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LOGINID:ssptacer1614

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

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 NEWS  1          Web Page for STN Seminar Schedule - N. America
 NEWS  2  OCT 02  CA/CAplus enhanced with pre-1907 records from Chemisches
                  Zentralblatt
 NEWS  3  OCT 19  BEILSTEIN updated with new compounds
 NEWS  4  NOV 15  Derwent Indian patent publication number format enhanced
 NEWS  5  NOV 19  WPIX enhanced with XML display format
 NEWS  6  NOV 30  ICSD reloaded with enhancements
 NEWS  7  DEC 04  LINPADOCDB now available on STN
 NEWS  8  DEC 14  BEILSTEIN pricing structure to change
 NEWS  9  DEC 17  USPATOLD added to additional database clusters
 NEWS 10  DEC 17  IMSDRUGCONF removed from database clusters and STN
 NEWS 11  DEC 17  DGENE now includes more than 10 million sequences
 NEWS 12  DEC 17  TOXCENTER enhanced with 2008 MeSH vocabulary in
                  MEDLINE segment
 NEWS 13  DEC 17  MEDLINE and LMEDLINE updated with 2008 MeSH vocabulary
 NEWS 14  DEC 17  CA/CAplus enhanced with new custom IPC display formats
 NEWS 15  DEC 17  STN Viewer enhanced with full-text patent content
                  from USPATOLD
 NEWS 16  JAN 02  STN pricing information for 2008 now available
 NEWS 17  JAN 16  CAS patent coverage enhanced to include exemplified
                  prophetic substances
 NEWS 18  JAN 28  USPATFULL, USPAT2, and USPATOLD enhanced with new
                  custom IPC display formats
 NEWS 19  JAN 28  MARPAT searching enhanced
 NEWS 20  JAN 28  USGENE now provides USPTO sequence data within 3 days
                  of publication
 NEWS 21  JAN 28  TOXCENTER enhanced with reloaded MEDLINE segment
 NEWS 22  JAN 28  MEDLINE and LMEDLINE reloaded with enhancements
 NEWS 23  FEB 08  STN Express, Version 8.3, now available
 NEWS 24  FEB 20  PCI now available as a replacement to DPCI
 NEWS 25  FEB 25  IFIREF reloaded with enhancements
 NEWS 26  FEB 25  IMSPRODUCT reloaded with enhancements
 NEWS 27  FEB 29  WPINDEX/WPIDS/WPIX enhanced with ECLA and current
                  U.S. National Patent Classification


 NEWS EXPRESS FEBRUARY 08 CURRENT WINDOWS VERSION IS V8.3,
              AND CURRENT DISCOVER FILE IS DATED 20 FEBRUARY 2008

 NEWS HOURS    STN Operating Hours Plus Help Desk Availability
 NEWS LOGIN    Welcome Banner and News Items
 NEWS IPC8     For general information regarding STN implementation of IPC 8
```

Enter NEWS followed by the item number or name to see news on that
specific topic.

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* * * * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 11:38:10 ON 03 MAR 2008

=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 11:38:21 ON 03 MAR 2008
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 2 MAR 2008 HIGHEST RN 1006303-40-7
DICTIONARY FILE UPDATES: 2 MAR 2008 HIGHEST RN 1006303-40-7

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH January 9, 2008.

Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

=> e us2006-554299/apps
'APPS' IS NOT A VALID EXPAND FIELD CODE FOR FILE 'REGISTRY'
The indicated field code is not available for EXPAND in this file. To see a list of valid EXPAND field codes, enter HELP SFIELDS at an arrow prompt (=>).

=> e us2006-554299/apps
'APPS' IS NOT A VALID EXPAND FIELD CODE FOR FILE 'REGISTRY'
The indicated field code is not available for EXPAND in this file. To see a list of valid EXPAND field codes, enter HELP SFIELDS at an arrow prompt (=>).

=> e us2006-554299/aps
'APS' IS NOT A VALID EXPAND FIELD CODE FOR FILE 'REGISTRY'
The indicated field code is not available for EXPAND in this file. To see a list of valid EXPAND field codes, enter HELP SFIELDS at an arrow prompt (=>).

=> e us2006-554299/apps
'APPS' IS NOT A VALID EXPAND FIELD CODE FOR FILE 'REGISTRY'
The indicated field code is not available for EXPAND in this

file. To see a list of valid EXPAND field codes, enter HELP
SFIELDS at an arrow prompt (=>).

=> file caplus
COST IN U.S. DOLLARS   SINCE FILE   TOTAL
                                                         ENTRY   SESSION
FULL ESTIMATED COST   1.38   1.59

FILE 'CAPLUS' ENTERED AT 11:39:58 ON 03 MAR 2008
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 3 Mar 2008 VOL 148 ISS 10
FILE LAST UPDATED: 2 Mar 2008 (20080302/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply.
They are available for your review at:

http://www.cas.org/infopolicy.html

=> e us2006-554299/apps
E1   1   US2006-554294/AP
E2   1   US2006-554295/AP
E3   1 --> US2006-554299/AP
E4   0   US2006-554299/PRN
E5   1   US2006-554300/AP
E6   1   US2006-554301/AP
E7   1   US2006-554302/AP
E8   1   US2006-554309/AP
E9   1   US2006-554309/PRN
E10   1   US2006-554312/AP
E11   1   US2006-554314/AP
E12   1   US2006-554315/AP

=> s e3
L1   1 US2006-554299/AP

=> d scan l1

L1   1 ANSWERS   CAPLUS COPYRIGHT 2008 ACS on STN
IC   ICM A61K031-445
     ICS A61K031-505
CC   1-8 (Pharmacology)
TI   Methods for prophylactic pretreatment of ischemic diseases with nitroxides
ST   treatment ischemia disease nitroxide antiischemic
IT   Drug delivery systems
        (injections, i.v.; methods for prophylactic pretreatment of ischemic
        diseases with nitroxides)
IT   Aneurysm

```
     Anti-ischemic agents
     Hemorrhage
     Human
     Ischemia
        (methods for prophylactic pretreatment of ischemic diseases with
        nitroxides)
IT   Drug delivery systems
        (oral; methods for prophylactic pretreatment of ischemic diseases with
        nitroxides)
IT   2226-96-2, 4-Hydroxy-2,2,6,6-tetramethylpiperidine-1-oxyl   13408-29-2,
     Nitroxide
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (methods for prophylactic pretreatment of ischemic diseases with
        nitroxides)

ALL ANSWERS HAVE BEEN SCANNED


=>  sel rn l1
E1 THROUGH E2 ASSIGNED

=> file reg
COST IN U.S. DOLLARS                            SINCE FILE      TOTAL
                                                     ENTRY    SESSION
FULL ESTIMATED COST                                   3.17       4.76

FILE 'REGISTRY' ENTERED AT 11:41:25 ON 03 MAR 2008
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:    2 MAR 2008  HIGHEST RN 1006303-40-7
DICTIONARY FILE UPDATES:   2 MAR 2008  HIGHEST RN 1006303-40-7

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH January 9, 2008.

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document.  For information
on property searching in REGISTRY, refer to:

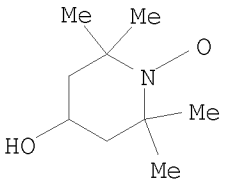
http://www.cas.org/support/stngen/stndoc/properties.html

=> s e1-e2
             1 13408-29-2/BI
               (13408-29-2/RN)
             1 2226-96-2/BI
               (2226-96-2/RN)
L2           2 (13408-29-2/BI OR 2226-96-2/BI)

=> d scan l2

L2   2 ANSWERS   REGISTRY  COPYRIGHT 2008 ACS on STN
```

IN 1-Piperidinyloxy, 4-hydroxy-2,2,6,6-tetramethyl-
ADDITIONAL NAMES NOT AVAILABLE IN THIS FORMAT
MF C9 H18 N O2
CI COM



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1

L2 2 ANSWERS REGISTRY COPYRIGHT 2008 ACS on STN
IN Nitroxide (7CI, 8CI, 9CI)
MF H2 N O
CI COM

H_2N-O

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

ALL ANSWERS HAVE BEEN SCANNED

=> s 13408-29-2
L3 1 13408-29-2
    (13408-29-2/RN)

=> s 2226-96-2
L4 1 2226-96-2
    (2226-96-2/RN)

=> file caplus biosis embase medline

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.92	5.68

FILE 'CAPLUS' ENTERED AT 11:42:52 ON 03 MAR 2008
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE 'BIOSIS' ENTERED AT 11:42:52 ON 03 MAR 2008

FILE 'EMBASE' ENTERED AT 11:42:52 ON 03 MAR 2008

FILE 'MEDLINE' ENTERED AT 11:42:52 ON 03 MAR 2008

```
=> s l3 or l4
L5        7167 L3 OR L4

=> e ischemia
E1           2     ISCHEMEMIA/BI
E2          52     ISCHEMI/BI
E3      510858 --> ISCHEMIA/BI
E4           5     ISCHEMIA1/BI
E5           3     ISCHEMIA2/BI
E6           2     ISCHEMIA3/BI
E7           1     ISCHEMIAA/BI
E8           1     ISCHEMIAAND/BI
E9          10     ISCHEMIAC/BI
E10          1     ISCHEMIACTION/BI
E11          1     ISCHEMIADISEASE/BI
E12          2     ISCHEMIADRIVEN/BI

=> s e3
L6       511008 ISCHEMIA/BI

=> e administration
E1           4     ADMINISTRATIOM/BI
E2           1     ADMINISTRATIOMN/BI
E3     4191846 --> ADMINISTRATION/BI
E4           1     ADMINISTRATION4/BI
E5           1     ADMINISTRATIONABBREVIATED/BI
E6          34     ADMINISTRATIONAL/BI
E7           1     ADMINISTRATIONALTHOUGH/BI
E8           4     ADMINISTRATIONAND/BI
E9           1     ADMINISTRATIONAPPROVED/BI
E10          1     ADMINISTRATIONAT/BI
E11          1     ADMINISTRATIONATION/BI
E12          2     ADMINISTRATIONB/BI

=> s e3
L7     4202108 ADMINISTRATION/BI

=> s (("medical treatment") or ("medical procedure?")) and l6
L8         1552 (("MEDICAL TREATMENT") OR ("MEDICAL PROCEDURE?")) AND L6

=> s l8 and l5
L9            0 L8 AND L5

=> s l5 and l8
L10           0 L5 AND L8

=> s l5 and ischemia
L11         245 L5 AND ISCHEMIA

=> s l11 and administration
L12          63 L11 AND ADMINISTRATION

=> s l12 and (intravenous or parenteral0
UNMATCHED LEFT PARENTHESIS 'AND (INTRAVENOU'
The number of right parentheses in a query must be equal to the
number of left parentheses.

=> s l12 and (intravenous or parenteral)
L13          28 L12 AND (INTRAVENOUS OR PARENTERAL)
```

```
=> s l12 and ((oral or orally) or ("by mouth"))
L14          9 L12 AND ((ORAL OR ORALLY) OR ("BY MOUTH"))

=> s l14 and l13
L15          4 L14 AND L13

=> d l15 1-4 hitstr ibib all
'HITSTR' IS NOT A VALID FORMAT FOR FILE 'EMBASE'

The following are valid formats:

The default display format is BIB.

ABS --------- AB
ALL --------- AN, TI, AU, CS, SO, PUI, CY, DT, FS, NCT, LA, SL, ED,
                 AB, CT, RN, CN, NP, CO,  GEN
BIB --------- AN, TI, AU, CS, SO, PUI, CY, DT, FS, NCT, LA, SL, ED
CBIB -------- Compressed bibliographic data
DALL -------- ALL, delimited for post-processing
IABS -------- ABS, with a text label
IALL -------- ALL, indented with text labels
IBIB -------- BIB, indented with text labels
IND --------- CT, RN, CN, NP, CO, GEN
TRIAL ------  TI, CT, RN, CN, NP, CO, GEN
 (SAM, TRI, FREE)
HIT --------- All fields containing hit terms
HITIND ------ IND
KWIC -------- All hit terms plus 20 words on either side
OCC --------- List of display fields containing hit terms
              and number of occurrences in each field

Hit terms will be highlighted in all displayable fields.

To display a particular field or fields,  enter the display field
codes.  For a list of display field codes, enter 'HELP DFIELDS'
at an arrow prompt (=>).  Examples of formats include: 'BIB';
'AB'; 'SO,AB'.  You may specify the format fields in any order,
and the information will be displayed in the same order as the
format specification.

The same formats (except for HIT, HITIND, KWIC, and OCC) may be
used with the DISPLAY ACC command to display the record for a
specified Accession Number.

ENTER DISPLAY FORMAT (BIB):ibib all

L15  ANSWER 1 OF 4  EMBASE  COPYRIGHT (c) 2008 Elsevier B.V. All rights
     reserved on STN
ACCESSION NUMBER:   2008088769  EMBASE
TITLE:              Antioxidants and free radical seavengers for the treatment
                    of stroke, traumatic brain injury and aging.
AUTHOR:             Slemmer J.E.; Shacka J.J.; Sweeney M.I.; Weber J.T.
CORPORATE SOURCE:   J.T. Weber, School of Pharmacy, Health Sciences Centre,
                    Memorial University of Newfoundland, 300 Prince Philip
                    Drive, St. John's, NL A1B 3V6, Canada. jweber@mun.ca
SOURCE:             Current Medicinal Chemistry, (Feb 2008) Vol. 15, No. 4, pp.
                    404-414.
                    Refs: 225
                    ISSN: 0929-8673  CODEN: CMCHE7
COUNTRY:            Netherlands
DOCUMENT TYPE:      Journal; General Review; (Review)
```

FILE SEGMENT: 030 Clinical and Experimental Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 3 Mar 2008
Last Updated on STN: 3 Mar 2008

AN 2008088769 EMBASE

TI Antioxidants and free radical seavengers for the treatment of stroke, traumatic brain injury and aging.

AU Slemmer J.E.; Shacka J.J.; Sweeney M.I.; Weber J.T.

CS J.T. Weber, School of Pharmacy, Health Sciences Centre, Memorial University of Newfoundland, 300 Prince Philip Drive, St. John's, NL A1B 3V6, Canada. jweber@mun.ca

SO Current Medicinal Chemistry, (Feb 2008) Vol. 15, No. 4, pp. 404-414.
Refs: 225
ISSN: 0929-8673 CODEN: CMCHE7

CY Netherlands

DT Journal; General Review; (Review)

FS 030 Clinical and Experimental Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
008 Neurology and Neurosurgery

LA English

SL English

ED Entered STN: 3 Mar 2008
Last Updated on STN: 3 Mar 2008

AB The overproduction of reactive oxygen species (ROS) and reactive nitrogen species (RNS) is a common underlying mechanism of many neuropathologies, as they have been shown to damage various cellular components, including proteins, lipids and DNA. Free radicals, especially superoxide (O(2)), and non-radicals, such as hydrogen peroxide (H(2)O(2)), can be generated in quantities large enough to overwhelm endogenous protective enzyme systems, such as superoxide dismutase (SOD) and reduced glutathione (GSH). Here we review the mechanisms of ROS and RNS prqduction, and their roles in ischemia, tramatic brain injury and aging. In.particular, we discuss several acute and chronic pharmacological therapies that have been extensively studied in order to reduce ROS/RNS loads in cells and the subsequent oxidative stress, so-called "free-radical scavengers." Although the overall aim has been to counteract the detrimental effects of ROS/RNS in these pathologies, success has been limited especially in human clinical studies. This review highlights some of the recent successes and failures in animal and human studies by attempting to link a compound's chemical structure with its efficacy as a free radical scavenger. In particular, we demonstrate how antioxidants derived from natural products, as well as long-term dietary alterations, may prove to be effective scavengers of ROS and RNS. .COPYRGT. 2008 Bentham Science Publishers Ltd.

CT Medical Descriptors:
*aging
brain hemorrhage: SI, side effect
cerebrovascular accident: DT, drug therapy
chemical structure
clinical trial
diet
drug conjugation
drug efficacy
human
ischemia
neurologic disease: ET, etiology
nonhuman

oxidative stress
pathophysiology
review
*stroke: DT, drug therapy
*traumatic brain injury: DT, drug therapy
CT Drug Descriptors:
acetylsalicylic acid: DT, drug therapy
acetylsalicylic acid: PO, oral drug administration
alpha tocopherol: CT, clinical trial
alpha tocopherol: PD, pharmacology
alteplase: AE, adverse drug reaction
alteplase: CB, drug combination
alteplase: DT, drug therapy
*antioxidant
cell protein: EC, endogenous compound
disufenton sodium: CT, clinical trial
disufenton sodium: CB, drug combination
disufenton sodium: DT, drug therapy
disufenton sodium: IV, intravenous drug administration
disufenton sodium: PD, pharmacology
DNA: EC, endogenous compound
enzyme inhibitor: DT, drug therapy
flavonoid
free radical: EC, endogenous compound
glutathione: EC, endogenous compound
hydrogen peroxide: EC, endogenous compound
lipid: EC, endogenous compound
lubeluzole: DT, drug therapy
lubeluzole: PD, pharmacology
natural product
nitric oxide synthase inhibitor: DT, drug therapy
nitroxide: DT, drug therapy
nitroxide: PD, pharmacology
nonsteroid antiinflammatory agent: PD, pharmacology
oxyresveratrol: AN, drug analysis
oxyresveratrol: DT, drug therapy
oxyresveratrol: PD, pharmacology
placebo
reactive nitrogen species: EC, endogenous compound
reactive oxygen metabolite: EC, endogenous compound
*scavenger: EC, endogenous compound
stilbene derivative: AN, drug analysis
stilbene derivative: DT, drug therapy
stilbene derivative: PD, pharmacology
superoxide: EC, endogenous compound
superoxide dismutase: CB, drug combination
superoxide dismutase: EC, endogenous compound
superoxide dismutase inhibitor: DT, drug therapy
tempol: DT, drug therapy
tirilazad: CT, clinical trial
tirilazad: DT, drug therapy
tirilazad: PD, pharmacology
unindexed drug
RN (acetylsalicylic acid) 493-53-8, 50-78-2, 53663-74-4, 53664-49-6, 63781-77-1; (alpha tocopherol) 1406-18-4, 1406-70-8, 52225-20-4, 58-95-7, 59-02-9; (alteplase) 105857-23-6; (disufenton sodium) 168021-79-2; (DNA) 9007-49-2; (glutathione) 70-18-8; (hydrogen peroxide) 7722-84-1; (lipid) 66455-18-3; (lubeluzole) 144665-07-6; (nitroxide) 13408-29-2; (superoxide dismutase) 37294-21-6, 9016-01-7, 9054-89-1; (superoxide) 11062-77-4; (tempol) 2226-96-2; (tirilazad) 110101-66-1, 110101-67-2, 111793-42-1

CN aspirin; nxy 059

L15 ANSWER 2 OF 4 EMBASE COPYRIGHT (c) 2008 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2007418201 EMBASE
TITLE: Hemigramicidin-TEMPO conjugates: Novel mitochondria-targeted antioxidants.
AUTHOR: Fink M.P.; Macias C.A.; Xiao J.; Tyurina Y.Y.; Delude R.L.; Greenberger J.S.; Kagan V.E.; Wipf P.
CORPORATE SOURCE: Dr. M.P. Fink, Department of Critical Care Medicine, University of Pittsburgh, Pittsburgh, PA, United States. finkmp@ccm.upmc.edu
SOURCE: Critical Care Medicine, (Sep 2007) Vol. 35, No. 9 SUPPL., pp. S461-S467.
Refs: 50
ISSN: 0090-3493 CODEN: CCMDC7
PUBLISHER IDENT.: 00003246200709001000006
COUNTRY: United States
DOCUMENT TYPE: Journal; Conference Article; (Conference paper)
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
030 Clinical and Experimental Pharmacology
037 Drug Literature Index
008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 25 Sep 2007
Last Updated on STN: 25 Sep 2007

AN 2007418201 EMBASE
TI Hemigramicidin-TEMPO conjugates: Novel mitochondria-targeted antioxidants.
AU Fink M.P.; Macias C.A.; Xiao J.; Tyurina Y.Y.; Delude R.L.; Greenberger J.S.; Kagan V.E.; Wipf P.
CS Dr. M.P. Fink, Department of Critical Care Medicine, University of Pittsburgh, Pittsburgh, PA, United States. finkmp@ccm.upmc.edu
SO Critical Care Medicine, (Sep 2007) Vol. 35, No. 9 SUPPL., pp. S461-S467.
Refs: 50
ISSN: 0090-3493 CODEN: CCMDC7
PUI 00003246200709001000006
CY United States
DT Journal; Conference Article; (Conference paper)
FS 018 Cardiovascular Diseases and Cardiovascular Surgery
030 Clinical and Experimental Pharmacology
037 Drug Literature Index
008 Neurology and Neurosurgery
LA English
SL English
ED Entered STN: 25 Sep 2007
Last Updated on STN: 25 Sep 2007
AB Reactive oxygen species (ROS) are reactive, partially reduced derivatives of molecular oxygen. ROS are important in the pathogenesis of a wide range of acute pathologic processes, including ischemia /reperfusion injury, sepsis, and shock. Accordingly, effective ROS scavengers might be useful therapeutic agents for these conditions. Since mitochondria are the primary sites for ROS production within cells, it seems reasonable that targeting ROS scavengers to these organelles could be a particularly effective strategy. Indeed, a number of compounds or classes of compounds have been described that are based on this concept. One approach consists of coupling a payload-the portion of the molecule with ROS-scavenging activities-to a targeting moiety-the portion of the molecule that promotes selective accumulation within mitochondria. For example, the payload portion of XJB-5-131 consists of a stable nitroxide radical, which has been extensively investigated as a cytoprotective agent

in a number of experimental models of oxidative stress. The targeting portion of XJB-5-131 consists of a portion of the membrane-active cyclopeptide antibiotic, gramicidin S. The gramicidin segment was used to target the nitroxide payload to mitochondria because antibiotics of this type have a high affinity for bacterial membranes and because of the close relationship between bacteria and mitochondria. In a rat model of hemorrhagic shock, delayed treatment with XJB-5-131 has been shown to prolong survival time in the absence of resuscitation with blood or a large volume of crystalloid fluid. Compounds like XJB-5-131 warrant further evaluation for the treatment of hemorrhagic shock as well as other acute conditions associated with increased mitochondrial production of ROS. .COPYRGT. 2007 Lippincott Williams & Wilkins, Inc.

CT Medical Descriptors:
bacterial membrane
binding affinity
blood volume
brain infarction: DT, drug therapy
cell culture
cell protection
conference paper
crystalloid
eukaryotic cell
  heart muscle ischemia: DT, drug therapy
heart muscle reperfusion
*hemorrhagic shock: DT, drug therapy
human
hypoxia
inflammation: DT, drug therapy
microangiopathy
mitochondrion
nonhuman
oxidative stress
priority journal
prokaryotic cell
resuscitation
stroke
survival time

CT Drug Descriptors:
10 (6' ubiquinolyl)decyltriphenylphosphonium bromide: DT, drug therapy
  10 (6' ubiquinolyl)decyltriphenylphosphonium bromide: PO, oral drug administration
10 (6' ubiquinolyl)decyltriphenylphosphonium bromide: PD, pharmacology
[2 (3,4 dihydro 6 hydroxy 2,5,7,8 tetramethyl 2h 1 benzopyran 2 yl)ethyl]triphenylphosphonium bromide: PD, pharmacology
antibiotic agent: DV, drug development
antibiotic agent: DT, drug therapy
antibiotic agent: PD, pharmacology
antioxidant: DT, drug therapy
  antioxidant: PO, oral drug administration
antioxidant: PD, pharmacology
cyclopeptide
*gramicidin: DV, drug development
*gramicidin: DT, drug therapy
  *gramicidin: IV, intravenous drug administration
*gramicidin: PD, pharmacology
gramicidin S
mitoq
mitoquinol
mitovit e
phospholipid: EC, endogenous compound
*piperidine derivative: DV, drug development

*piperidine derivative: DT, drug therapy
*piperidine derivative: IV, intravenous drug administration
*piperidine derivative: PD, pharmacology
reactive oxygen metabolite: EC, endogenous compound
ss 31: DT, drug therapy
ss 31: PD, pharmacology
tempol: CM, drug comparison
tempol: DT, drug therapy
tempol: PD, pharmacology
*xjb 5 125: DV, drug development
*xjb 5 125: PD, pharmacology
*xjb 5 131: CM, drug comparison
*xjb 5 131: DV, drug development
*xjb 5 131: DT, drug therapy
*xjb 5 131: IV, intravenous drug administration
*xjb 5 131: PD, pharmacology
xjb 5131
RN (gramicidin S) 113-73-5, 15207-30-4, 17174-97-9, 57572-76-6; (gramicidin) 1405-97-6; (tempol) 2226-96-2
CN mitoq; mitoquinol; mitovit e; ss 31; tempol; xjb 5131

L15 ANSWER 3 OF 4 EMBASE COPYRIGHT (c) 2008 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2007159512 EMBASE
TITLE: Nitric oxide: Ocular blood flow, glaucoma, and diabetic retinopathy.
AUTHOR: Toda N.; Nakanishi-Toda M.
CORPORATE SOURCE: N. Toda, Toyama Institute for Cardiovascular Pharmacology Research, 7-13, 1-Chome, Azuchi-machi, Chuo-ku, Osaka, Japan. n.toda.toyama-bldg@orion.ocn.ne.jp
SOURCE: Progress in Retinal and Eye Research, (May 2007) Vol. 26, No. 3, pp. 205-238.
Refs: 370
ISSN: 1350-9462 CODEN: PRTRES
PUBLISHER IDENT.: S 1350-9462(07)00005-5
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 012 Ophthalmology
037 Drug Literature Index
005 General Pathology and Pathological Anatomy
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 14 May 2007
Last Updated on STN: 14 May 2007
AN 2007159512 EMBASE
TI Nitric oxide: Ocular blood flow, glaucoma, and diabetic retinopathy.
AU Toda N.; Nakanishi-Toda M.
CS N. Toda, Toyama Institute for Cardiovascular Pharmacology Research, 7-13, 1-Chome, Azuchi-machi, Chuo-ku, Osaka, Japan. n.toda.toyama-bldg@orion.ocn.ne.jp
SO Progress in Retinal and Eye Research, (May 2007) Vol. 26, No. 3, pp. 205-238.
Refs: 370
ISSN: 1350-9462 CODEN: PRTRES
PUI S 1350-9462(07)00005-5
CY United Kingdom
DT Journal; General Review; (Review)
FS 012 Ophthalmology
037 Drug Literature Index
005 General Pathology and Pathological Anatomy
LA English

SL English
ED Entered STN: 14 May 2007
Last Updated on STN: 14 May 2007
AB Nitric oxide (NO) is widely recognized to be quite an important intercellular messenger in the cardiovascular and nervous systems or immunological reactions, including that in the eye. This molecule formed by constitutive NO synthase (NOS), endothelial (eNOS) and neuronal (nNOS), contributes to physiologically regulate ocular hemodynamics and cell viability and protects vascular endothelial cells and nerve cells or fibers against pathogenic factors associated with glaucoma, ischemia, and diabetes mellitus. Ocular blood flow is regulated by NO derived from the endothelium and efferent nitrergic neurons. Endothelial dysfunction impairs ocular hemodynamics by reducing the bioavailability of NO and increasing the production of reactive oxygen species (ROS). On the other hand, NO formed by inducible NOS (iNOS) expressed under influences of inflammatory mediators evokes neurodegeneration and cell apoptosis, leading to serious ocular diseases. NO over-produced by nNOS in the retina stimulated by excitotoxic amino acids or exposed to ischemia also mediates retinal injury. Because of these dichotomous roles of NO, which has both beneficial and pathogenic actions, one may face difficulties in constructing therapeutic strategies with NO supplementation or NOS inhibition. Up-to-date information concerning physiological roles of NO produced by the different NOS isoforms in the eye and interactions between NO and glaucoma, retinal ischemia, or diabetic retinopathy would help clinicians to select a valid pharmacological therapy that would be appropriate for a specific ocular disease.
CT Medical Descriptors:
apoptosis
cell viability
diabetes mellitus
*diabetic retinopathy: ET, etiology
endothelial dysfunction
enzyme inhibition
*eye blood flow
*glaucoma: DT, drug therapy
*glaucoma: ET, etiology
hemodynamics
histopathology
human
hyperoxia
hypoxia
immunity
inflammation
innervation
intraocular hypertension: DT, drug therapy
ischemia: ET, etiology
molecular interaction
nerve cell
nerve degeneration: ET, etiology
neuroprotection
nitrergic nerve
nonhuman
priority journal
protein expression
retina
retina injury
retina ischemia
retinopathy
review
risk factor

vasodilatation
CT Drug Descriptors:
2,3 dihydro 5 methyl 3 (morpholinomethyl) 6 (1 naphthoyl)pyrrolo[1,2,3 de][1,4]benzoxazine
7 nitroindazole: DT, drug therapy
7 nitroindazole: IP, intraperitoneal drug administration
7 nitroindazole: PD, pharmacology
arginine: PD, pharmacology
bradykinin
cyclic GMP: EC, endogenous compound
dizocilpine
dronabinol
endothelium derived relaxing factor: EC, endogenous compound
glyceryl trinitrate: DT, drug therapy
glyceryl trinitrate: IV, intravenous drug administration
glyceryl trinitrate: TP, topical drug administration
hydralazine: DT, drug therapy
indometacin
inducible nitric oxide synthase: EC, endogenous compound
isoenzyme: EC, endogenous compound
isosorbide dinitrate: DT, drug therapy
isosorbide dinitrate: PO, oral drug administration
linsidomine: DT, drug therapy
linsidomine: TP, topical drug administration
n methyl dextro aspartic acid receptor blocking agent
n(g) methylarginine: DT, drug therapy
n(g) methylarginine: IV, intravenous drug administration
n(g) methylarginine: VI, intravitreal drug administration
n(g) methylarginine: PD, pharmacology
n(g) nitroarginine: DT, drug therapy
n(g) nitroarginine: PD, pharmacology
n(g) nitroarginine methyl ester: DT, drug therapy
n(g) nitroarginine methyl ester: IV, intravenous drug administration
n(g) nitroarginine methyl ester: PD, pharmacology
n(g),n(g) dimethylarginine: DT, drug therapy
n(g),n(g) dimethylarginine: PD, pharmacology
neuronal nitric oxide synthase: EC, endogenous compound
nipradilol
*nitric oxide: DT, drug therapy
nitric oxide synthase inhibitor: DT, drug therapy
nitric oxide synthase inhibitor: PD, pharmacology
nitroprusside sodium: DT, drug therapy
reactive oxygen metabolite: EC, endogenous compound
SNARE protein: DT, drug therapy
SNARE protein: TP, topical drug administration
tempol
unindexed drug
vasculotropin: EC, endogenous compound
RN (2,3 dihydro 5 methyl 3 (morpholinomethyl) 6 (1 naphthoyl)pyrrolo[1,2,3 de][1,4]benzoxazine) 134959-51-6; (7 nitroindazole) 2942-42-9; (arginine) 1119-34-2, 15595-35-4, 7004-12-8, 74-79-3; (bradykinin) 58-82-2, 5979-11-3; (cyclic GMP) 7665-99-8; (dizocilpine) 77086-21-6; (dronabinol) 7663-50-5; (endothelium derived relaxing factor) 90880-94-7; (glyceryl trinitrate) 55-63-0; (hydralazine) 304-20-1, 86-54-4; (indometacin) 53-86-1, 74252-25-8, 7681-54-1; (inducible nitric oxide synthase) 501433-35-8; (isosorbide dinitrate) 87-33-2; (linsidomine) 16142-27-1, 33876-97-0; (n(g) methylarginine) 156706-47-7, 17035-90-4; (n(g) nitroarginine methyl ester) 50903-99-6; (n(g) nitroarginine) 2149-70-4; (n(g),n(g) dimethylarginine) 30315-93-6; (neuronal nitric oxide synthase) 506430-87-1; (nipradilol) 81486-22-8; (nitric oxide) 10102-43-9;

(nitroprusside sodium) 14402-89-2, 15078-28-1; (tempol) 2226-96-2 ; (vasculotropin) 127464-60-2

L15 ANSWER 4 OF 4 EMBASE COPYRIGHT (c) 2008 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2006354644 EMBASE
TITLE: Lack of long-term protective effect of antioxidant/anti-inflammatory therapy in transplant-induced ischemia /reperfusion injury.
AUTHOR: Tain Y.-L.; Muller V.; Szabo A.; Dikalova A.; Griendling K.; Baylis C.
CORPORATE SOURCE: Dr. Y.-L. Tain, Department of Physiology and Functional Genomics, University of Florida, POB 100274, Gainesville, FL 32611, United States. tainyl@ufl.edu
SOURCE: American Journal of Nephrology, (Jul 2006) Vol. 26, No. 3, pp. 213-217.
Refs: 15
ISSN: 0250-8095 CODEN: AJNED9
COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 028 Urology and Nephrology
030 Clinical and Experimental Pharmacology
037 Drug Literature Index
005 General Pathology and Pathological Anatomy
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 22 Aug 2006
Last Updated on STN: 22 Aug 2006

AN 2006354644 EMBASE
TI Lack of long-term protective effect of antioxidant/anti-inflammatory therapy in transplant-induced ischemia/reperfusion injury.
AU Tain Y.-L.; Muller V.; Szabo A.; Dikalova A.; Griendling K.; Baylis C.
CS Dr. Y.-L. Tain, Department of Physiology and Functional Genomics, University of Florida, POB 100274, Gainesville, FL 32611, United States. tainyl@ufl.edu
SO American Journal of Nephrology, (Jul 2006) Vol. 26, No. 3, pp. 213-217.
Refs: 15
ISSN: 0250-8095 CODEN: AJNED9
CY Switzerland
DT Journal; Article
FS 028 Urology and Nephrology
030 Clinical and Experimental Pharmacology
037 Drug Literature Index
005 General Pathology and Pathological Anatomy
LA English
SL English
ED Entered STN: 22 Aug 2006
Last Updated on STN: 22 Aug 2006
AB Background: Alloantigen-independent factors contribute to long-term damage in renal transplant recipients, likely due to ischemia /reperfusion (I/R) injury at transplantation (Tx). I/R injury promotes oxidative stress and inflammation resulting in endothelial injury. Methods: In this study we investigated the long-term efficacy (22 weeks) of short-term (10 day) endothelial protection therapy (EP) in 'optimal' donor kidneys using the male Fisher 344 rat isograft (ISO) model. ISO-EP kidneys were compared to untreated ISO (ISO-UN) kidneys. EP involved dexamethasone to donor, ex vivo treatment of the kidney with deferoxamine and tempol, and administration to the recipient of L-arginine and tempol for 10 days. Rats were sacrificed 22 weeks following Tx and compared to age-matched, normal controls. Results: Both groups of ISO Tx rats developed similar renal dysfunction and structural damage and renal

NADPH-oxidase- dependent O(2)(-) production was similarly elevated in ISO-UN and ISO-EP groups vs. controls. In vitro renal cortex NO synthase (NOS) activity was also similar in ISO-UN and ISO-EP rats, despite lower nNOS and eNOS protein abundance in ISO-EP. Conclusion: I/R injury-induced late graft dysfunction occurs even when optimal donors are used and when short-term EP treatment is given. Increased renal superoxide production is not prevented by short-term EP therapy.

CT Medical Descriptors:
animal experiment
animal model
animal tissue
article
controlled study
drug effect
drug efficacy
endothelium
enzyme activity
female
isograft
kidney cortex
kidney donor
kidney dysfunction: CO, complication
kidney dysfunction: DT, drug therapy
kidney dysfunction: PC, prevention
kidney injury: CO, complication
kidney injury: DT, drug therapy
kidney injury: PC, prevention
*kidney ischemia: CO, complication
*kidney ischemia: DT, drug therapy
*kidney ischemia: PC, prevention
kidney transplantation
long term care
male
nonhuman
priority journal
rat
rat strain
*reperfusion injury: CO, complication
*reperfusion injury: DT, drug therapy
*reperfusion injury: PC, prevention

CT Drug Descriptors:
antiinflammatory agent: DT, drug therapy
antiinflammatory agent: IV, intravenous drug administration
antiinflammatory agent: PD, pharmacology
antioxidant: DT, drug therapy
antioxidant: PD, pharmacology
*arginine: DT, drug therapy
*arginine: PD, pharmacology
*deferoxamine: PD, pharmacology
*dexamethasone: DT, drug therapy
*dexamethasone: IV, intravenous drug administration
*dexamethasone: PD, pharmacology
nitric oxide synthase: EC, endogenous compound
reduced nicotinamide adenine dinucleotide phosphate oxidase: EC, endogenous compound
superoxide: EC, endogenous compound
*tempol: DT, drug therapy
*tempol: PO, oral drug administration
*tempol: PD, pharmacology

RN (arginine) 1119-34-2, 15595-35-4, 7004-12-8, 74-79-3; (deferoxamine)

```
     70-51-9; (dexamethasone) 50-02-2; (nitric oxide synthase) 125978-95-2;
     (reduced nicotinamide adenine dinucleotide phosphate oxidase) 9032-22-8;
     (superoxide) 11062-77-4; (tempol) 2226-96-2
CO   app (United States); Fresenius (United States); Sigma Aldrich (United
     States)


=> d his

     (FILE 'HOME' ENTERED AT 11:38:10 ON 03 MAR 2008)

     FILE 'REGISTRY' ENTERED AT 11:38:21 ON 03 MAR 2008

     FILE 'CAPLUS' ENTERED AT 11:39:58 ON 03 MAR 2008
                E US2006-554299/APPS
L1            1 S E3
                SEL RN L1

     FILE 'REGISTRY' ENTERED AT 11:41:25 ON 03 MAR 2008
L2            2 S E1-E2
L3            1 S 13408-29-2
L4            1 S 2226-96-2

     FILE 'CAPLUS, BIOSIS, EMBASE, MEDLINE' ENTERED AT 11:42:52 ON 03 MAR 2008
L5         7167 S L3 OR L4
                E ISCHEMIA
L6       511008 S E3
                E ADMINISTRATION
L7      4202108 S E3
L8         1552 S (("MEDICAL TREATMENT") OR ("MEDICAL PROCEDURE?")) AND L6
L9            0 S L8 AND L5
L10           0 S L5 AND L8
L11         245 S L5 AND ISCHEMIA
L12          63 S L11 AND ADMINISTRATION
L13          28 S L12 AND (INTRAVENOUS OR PARENTERAL)
L14           9 S L12 AND ((ORAL OR ORALLY) OR ("BY MOUTH"))
L15           4 S L14 AND L13

=> s
ENTER LOGIC EXPRESSION, QUERY NAME, OR (END):s
L16    8476811 S

=> d his

     (FILE 'HOME' ENTERED AT 11:38:10 ON 03 MAR 2008)

     FILE 'REGISTRY' ENTERED AT 11:38:21 ON 03 MAR 2008

     FILE 'CAPLUS' ENTERED AT 11:39:58 ON 03 MAR 2008
                E US2006-554299/APPS
L1            1 S E3
                SEL RN L1

     FILE 'REGISTRY' ENTERED AT 11:41:25 ON 03 MAR 2008
L2            2 S E1-E2
L3            1 S 13408-29-2
L4            1 S 2226-96-2

     FILE 'CAPLUS, BIOSIS, EMBASE, MEDLINE' ENTERED AT 11:42:52 ON 03 MAR 2008
L5         7167 S L3 OR L4
                E ISCHEMIA
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L6       511008 S E3
                E ADMINISTRATION
L7      4202108 S E3
L8         1552 S (("MEDICAL TREATMENT") OR ("MEDICAL PROCEDURE?")) AND L6
L9            0 S L8 AND L5
L10           0 S L5 AND L8
L11         245 S L5 AND ISCHEMIA
L12          63 S L11 AND ADMINISTRATION
L13          28 S L12 AND (INTRAVENOUS OR PARENTERAL)
L14           9 S L12 AND ((ORAL OR ORALLY) OR ("BY MOUTH"))
L15           4 S L14 AND L13
L16     8476811 S  S

=> s l15 and surgery
L17           0 L15 AND SURGERY

=> s l14 and surgery
L18           0 L14 AND SURGERY

=> s l13 and surgery
L19           1 L13 AND SURGERY

=> s l12 and surgery
L20           1 L12 AND SURGERY

=> s l11 and surgery
L21           8 L11 AND SURGERY

=> d his

     (FILE 'HOME' ENTERED AT 11:38:10 ON 03 MAR 2008)

     FILE 'REGISTRY' ENTERED AT 11:38:21 ON 03 MAR 2008

     FILE 'CAPLUS' ENTERED AT 11:39:58 ON 03 MAR 2008
                E US2006-554299/APPS
L1            1 S E3
                SEL RN L1

     FILE 'REGISTRY' ENTERED AT 11:41:25 ON 03 MAR 2008
L2            2 S E1-E2
L3            1 S 13408-29-2
L4            1 S 2226-96-2

     FILE 'CAPLUS, BIOSIS, EMBASE, MEDLINE' ENTERED AT 11:42:52 ON 03 MAR 2008
L5         7167 S L3 OR L4
                E ISCHEMIA
L6       511008 S E3
                E ADMINISTRATION
L7      4202108 S E3
L8         1552 S (("MEDICAL TREATMENT") OR ("MEDICAL PROCEDURE?")) AND L6
L9            0 S L8 AND L5
L10           0 S L5 AND L8
L11         245 S L5 AND ISCHEMIA
L12          63 S L11 AND ADMINISTRATION
L13          28 S L12 AND (INTRAVENOUS OR PARENTERAL)
L14           9 S L12 AND ((ORAL OR ORALLY) OR ("BY MOUTH"))
L15           4 S L14 AND L13
L16     8476811 S  S
L17           0 S L15 AND SURGERY
L18           0 S L14 AND SURGERY
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L19           1 S L13 AND SURGERY
L20           1 S L12 AND SURGERY
L21           8 S L11 AND SURGERY

=> d l19 1 hitstr ibib all
'HITSTR' IS NOT A VALID FORMAT FOR FILE 'EMBASE'

The following are valid formats:

The default display format is BIB.

ABS --------- AB
ALL --------- AN, TI, AU, CS, SO, PUI, CY, DT, FS, NCT, LA, SL, ED,
                 AB, CT, RN, CN, NP, CO,  GEN
BIB --------- AN, TI, AU, CS, SO, PUI, CY, DT, FS, NCT, LA, SL, ED
CBIB -------- Compressed bibliographic data
DALL -------- ALL, delimited for post-processing
IABS -------- ABS, with a text label
IALL -------- ALL, indented with text labels
IBIB -------- BIB, indented with text labels
IND --------- CT, RN, CN, NP, CO, GEN
TRIAL ------  TI, CT, RN, CN, NP, CO, GEN
 (SAM, TRI, FREE)
HIT --------- All fields containing hit terms
HITIND ------ IND
KWIC -------- All hit terms plus 20 words on either side
OCC --------- List of display fields containing hit terms
              and number of occurrences in each field

Hit terms will be highlighted in all displayable fields.

To display a particular field or fields,  enter the display field
codes.  For a list of display field codes, enter 'HELP DFIELDS'
at an arrow prompt (=>).  Examples of formats include: 'BIB';
'AB'; 'SO,AB'.  You may specify the format fields in any order,
and the information will be displayed in the same order as the
format specification.

The same formats (except for HIT, HITIND, KWIC, and OCC) may be
used with the DISPLAY ACC command to display the record for a
specified Accession Number.

ENTER DISPLAY FORMAT (BIB):ibib all

L19  ANSWER 1 OF 1  EMBASE  COPYRIGHT (c) 2008 Elsevier B.V. All rights
     reserved on STN
ACCESSION NUMBER:   2000416423  EMBASE
TITLE:              Polynitroxyl albumin plus tempol attenuates liver injury
                    and inflammation after hepatic ischemia and
                    reperfusion.
AUTHOR:             Blonder J.M.; McCalden T.A.; Hsia C.J.C.; Billings R.E.
CORPORATE SOURCE:   J.M. Blonder, RxKinetix, Inc., 1172 Century Dr.,
                    Louisville, CO 80027, United States. joan@rxkinetix.com
SOURCE:             Life Sciences, (17 Nov 2000) Vol. 67, No. 26, pp.
                    3231-3239.
                    Refs: 32
                    ISSN: 0024-3205  CODEN: LIFSAK
PUBLISHER IDENT.:   S 0024-3205(00)00907-3
COUNTRY:            United States
DOCUMENT TYPE:      Journal; Article
FILE SEGMENT:       030     Clinical and Experimental Pharmacology
```

037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 14 Dec 2000
Last Updated on STN: 14 Dec 2000

AN 2000416423 EMBASE

TI Polynitroxyl albumin plus tempol attenuates liver injury and inflammation after hepatic ischemia and reperfusion.

AU Blonder J.M.; McCalden T.A.; Hsia C.J.C.; Billings R.E.

CS J.M. Blonder, RxKinetix, Inc., 1172 Century Dr., Louisville, CO 80027, United States. joan@rxkinetix.com

SO Life Sciences, (17 Nov 2000) Vol. 67, No. 26, pp. 3231-3239.
Refs: 32
ISSN: 0024-3205 CODEN: LIFSAK

PUI S 0024-3205(00)00907-3

CY United States

DT Journal; Article

FS 030 Clinical and Experimental Pharmacology
037 Drug Literature Index

LA English

SL English

ED Entered STN: 14 Dec 2000
Last Updated on STN: 14 Dec 2000

AB PNA+Tempol, albumin containing conjugated (polynitroxyl albumin; PNA) and free (4-hydroxyl-2,2,6,6-tetramethyl-piperidinyl-1-oxyl; Tempol) nitroxide may protect against injury caused by reactive oxygen species. Therefore, the actions of PNA+Tempol on liver injury and inflammation induced by hepatic ischemia and reperfusion (I/R) were examined. Rats were subjected to 1 h ischemia followed by 24 h reperfusion in the absence (I/R) or presence of PNA+Tempol (25%; 15 mL/kg, i.v.) (I/R+PNA+Tempol) or human serum albumin (23%; 13.5 mL/kg, i.v.) (I/R+HSA). Test solutions were administered prior to and for 2 h during reperfusion. Sham-operated rats underwent surgery with neither ischemia nor infusion. I/R+PNA+Tempol rats had significantly less liver injury and inflammation than I/R rats. I/R+PNA+Tempol livers exhibited focal lesions whereas I/R livers exhibited global necrosis. Likewise, plasma ALT activity was significantly lower in I/R+PNA+Tempol rats. PNA+Tempol reduced I/R-induced neutrophil accumulation and intercellular adhesion molecule-1 (ICAM-1) expression. HSA did not alter I/R-induced liver injury or inflammation. Sham-operated rats exhibited normal liver morphology and no inflammation. Attenuation of I/R liver injury by PNA+Tempol may be mediated by its effect on inflammation, the major contributor to I/R injury. Reduction of inflammation by PNA+Tempol is most likely due to the antioxidative nature of the nitroxides. (C) 2000 Elsevier Science Inc.

CT Medical Descriptors:
animal experiment
animal model
antioxidant activity
article
controlled study
enzyme activity
*hepatitis
immunohistochemistry
*liver injury
*liver ischemia
liver necrosis
liver protection
male
neutrophil
nonhuman

```
     *oxidative stress
     protein expression
     rat
     *reperfusion
CT   Drug Descriptors:
     alanine aminotransferase: EC, endogenous compound
       *human albumin: IV, intravenous drug administration
     intercellular adhesion molecule 1: EC, endogenous compound
       *nitroxide: IV, intravenous drug administration
     *reactive oxygen metabolite: EC, endogenous compound
       *tempol: IV, intravenous drug administration
RN   (alanine aminotransferase) 9000-86-6, 9014-30-6; (intercellular adhesion
     molecule 1) 126547-89-5; (nitroxide) 13408-29-2; (tempol)
     2226-96-2
CN   (1) buminate
CO   (1) Baxter (United States)


=> d his

     (FILE 'HOME' ENTERED AT 11:38:10 ON 03 MAR 2008)

     FILE 'REGISTRY' ENTERED AT 11:38:21 ON 03 MAR 2008

     FILE 'CAPLUS' ENTERED AT 11:39:58 ON 03 MAR 2008
                E US2006-554299/APPS
L1             1 S E3
                SEL RN L1

     FILE 'REGISTRY' ENTERED AT 11:41:25 ON 03 MAR 2008
L2             2 S E1-E2
L3             1 S 13408-29-2
L4             1 S 2226-96-2

     FILE 'CAPLUS, BIOSIS, EMBASE, MEDLINE' ENTERED AT 11:42:52 ON 03 MAR 2008
L5          7167 S L3 OR L4
                E ISCHEMIA
L6        511008 S E3
                E ADMINISTRATION
L7       4202108 S E3
L8          1552 S (("MEDICAL TREATMENT") OR ("MEDICAL PROCEDURE?")) AND L6
L9             0 S L8 AND L5
L10            0 S L5 AND L8
L11          245 S L5 AND ISCHEMIA
L12           63 S L11 AND ADMINISTRATION
L13           28 S L12 AND (INTRAVENOUS OR PARENTERAL)
L14            9 S L12 AND ((ORAL OR ORALLY) OR ("BY MOUTH"))
L15            4 S L14 AND L13
L16      8476811 S  S
L17            0 S L15 AND SURGERY
L18            0 S L14 AND SURGERY
L19            1 S L13 AND SURGERY
L20            1 S L12 AND SURGERY
L21            8 S L11 AND SURGERY

=> s l5 and surgery and intravenous
L22            4 L5 AND SURGERY AND INTRAVENOUS

=> dup rem l22 l21
PROCESSING COMPLETED FOR L22
PROCESSING COMPLETED FOR L21
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L23 8 DUP REM L22 L21 (4 DUPLICATES REMOVED)
ANSWERS '1-2' FROM FILE BIOSIS
ANSWERS '3-4' FROM FILE EMBASE
ANSWERS '5-7' FROM FILE CAPLUS
ANSWER '8' FROM FILE MEDLINE

=> d l23 1-8 hitstr ibib all

L23 ANSWER 1 OF 8 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
DUPLICATE 1
ACCESSION NUMBER: 2001:11150 BIOSIS
DOCUMENT NUMBER: PREV200100011150
TITLE: Polynitroxyl albumin plus tempol attenuates liver injury and inflammation after hepatic ischemia and reperfusion.
AUTHOR(S): Blonder, Joan M. [Reprint author]; McCalden, Thomas A.; Hsia, Carleton J. C.; Billings, Ruth E.
CORPORATE SOURCE: RxKinetix, Inc., 1172 Century Dr., Suite 260, Louisville, CO, 80027, USA
joan@rxkinetix.com
SOURCE: Life Sciences, (November, 2000) Vol. 67, No. 26, pp. 3231-3239. print.
CODEN: LIFSAK. ISSN: 0024-3205.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 21 Dec 2000
Last Updated on STN: 21 Dec 2000
AN 2001:11150 BIOSIS
DN PREV200100011150
TI Polynitroxyl albumin plus tempol attenuates liver injury and inflammation after hepatic ischemia and reperfusion.
AU Blonder, Joan M. [Reprint author]; McCalden, Thomas A.; Hsia, Carleton J. C.; Billings, Ruth E.
CS RxKinetix, Inc., 1172 Century Dr., Suite 260, Louisville, CO, 80027, USA
joan@rxkinetix.com
SO Life Sciences, (November, 2000) Vol. 67, No. 26, pp. 3231-3239. print.
CODEN: LIFSAK. ISSN: 0024-3205.
DT Article
LA English
ED Entered STN: 21 Dec 2000
Last Updated on STN: 21 Dec 2000
AB PNA+Tempol, albumin containing conjugated (polynitroxyl albumin; PNA) and free (4-hydroxyl-2,2,6,6-tetramethyl-piperidinyl-1-oxyl; Tempol) nitroxide may protect against injury caused by reactive oxygen species. Therefore, the actions of PNA+Tempol on liver injury and inflammation induced by hepatic ischemia and reperfusion (I/R) were examined. Rats were subjected to 1 h ischemia followed by 24 h reperfusion in the absence (I/R) or presence of PNA+Tempol (25%; 15 mL/kg, i.v.) (I/R+PNA+Tempol) or human serum albumin (23%; 13.5 mL/kg, i.v.) (I/R+HSA). Test solutions were administered prior to and for 2 h during reperfusion. Sham-operated rats underwent surgery with neither ischemia nor infusion. I/R+PNA+Tempol rats had significantly less liver injury and inflammation than I/R rats. I/R+PNA+Tempol livers exhibited focal lesions whereas I/R livers exhibited global necrosis. Likewise, plasma ALT activity was significantly lower in I/R+PNA+Tempol rats. PNA+Tempol reduced I/R-induced neutrophil accumulation and intercellular adhesion molecule-1 (ICAM-1) expression. HSA did not alter I/R-induced liver injury or inflammation. Sham-operated rats exhibited normal liver morphology and no inflammation. Attenuation of I/R liver injury by PNA+Tempol may be mediated by its effect on inflammation, the major contributor to I/R injury. Reduction of inflammation by PNA+Tempol

is most likely due to the antioxidative nature of the nitroxides.
CC Pharmacology - General 22002
Biochemistry studies - General 10060
Pathology - Therapy 12512
Digestive system - Physiology and biochemistry 14004
Cardiovascular system - Physiology and biochemistry 14504
Cardiovascular system - Blood vessel pathology 14508
IT Major Concepts
Digestive System (Ingestion and Assimilation); Pharmacology; Cardiovascular System (Transport and Circulation)
IT Parts, Structures, & Systems of Organisms
liver: digestive system
IT Diseases
ischemia: vascular disease
Ischemia (MeSH)
IT Diseases
reperfusion injury: vascular disease
Reperfusion Injury (MeSH)
IT Chemicals & Biochemicals
polynitroxyl albumin; reactive oxygen species; tempol
ORGN Classifier
Muridae 86375
Super Taxa
Rodentia; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
rat
Taxa Notes
Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Rodents, Vertebrates
RN 2226-96-2 (tempol)

L23 ANSWER 2 OF 8 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
ACCESSION NUMBER: 2007:332209 BIOSIS
DOCUMENT NUMBER: PREV200700329336
TITLE: Cardiovascular effects of tempol in renovascular hypertension.
AUTHOR(S): de Oliveira-Sales, Elizabeth Barbosa [Reprint Author]; Carrilo, Bruno Arruda; Nishi, Erika Emy; Martins, Paulo J.; D'Almeida, Vania
CORPORATE SOURCE: Univ Fed Sao Paulo, Sao Paulo, Brazil
SOURCE: FASEB Journal, (APR 2007) Vol. 21, No. 6, pp. A876. Meeting Info.: Experimental Biology 2007 Annual Meeting. Washington, DC, USA. April 28 -May 02, 2007. Amer Assoc Anatomists; Amer Physiol Soc; Amer Soc Biochem & Mol biol; Amer Soc Investigat Pathol; Amer Soc Nutr; Amer Soc Pharmacol & Expt Therapeut.
CODEN: FAJOEC. ISSN: 0892-6638.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 30 May 2007
Last Updated on STN: 30 May 2007
AN 2007:332209 BIOSIS
DN PREV200700329336
TI Cardiovascular effects of tempol in renovascular hypertension.
AU de Oliveira-Sales, Elizabeth Barbosa [Reprint Author]; Carrilo, Bruno Arruda; Nishi, Erika Emy; Martins, Paulo J.; D'Almeida, Vania
CS Univ Fed Sao Paulo, Sao Paulo, Brazil
SO FASEB Journal, (APR 2007) Vol. 21, No. 6, pp. A876. Meeting Info.: Experimental Biology 2007 Annual Meeting. Washington, DC, USA. April 28 -May 02, 2007. Amer Assoc Anatomists; Amer Physiol Soc; Amer

Soc Biochem & Mol biol; Amer Soc Investigat Pathol; Amer Soc Nutr; Amer Soc Pharmacol & Expt Therapeut.
CODEN: FAJOEC. ISSN: 0892-6638.

DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)

LA English

ED Entered STN: 30 May 2007
Last Updated on STN: 30 May 2007

AB The mechanisms for maintenance of renovascular hypertension remain undefined. Excess Angiotensin II generation may lead to release of reactive oxygen species and increased vasoconstrictor activity. the major aim of the present study was to evaluate the effects of acute intravenous (IV) administration of superoxide dismutase mimetic 4-hidroxy-2,?,6,6-tetramethylpiperidine-1-oxyl (Tempo]) on mean arterial blood pressure (MAP), heart rate (HR) and renal sympathetic nerve activity (RSNA) in the renovascular hypertension performed in mate Wistar rats (6 weeks after renal surgery - Goldblatt hypertension model 2K-1C). Moreover, to examine the oxidative stress in this model, blood samples were collected and measured with thiobarbituric acid-reactive substances (TBARS).Wistar rats were divided in control group (C, n=13) and hypertensive group (2K-1C, n=14). Tempol was infused (10 and 30mg/kg, IV, 6 min.) and MAP, HR and RSNA were monitored for 30 minutes. Acute Tempol treatment (10 mg/kg) in hypertensive rats produced a. decrease in MAP (7 +/- 1%) during infusion followed by a significant decrease in RSNA (8 +/- 2%, p < 0,02), with no changes,in HR ' Tempol 30mg/kg reduced significantly MAP by 23 4%, p < 0,001 in 2K- I C and the RSNA decreased 17 +/- 7%, p < 0,04. In normotensives rats, Tempol 10mg/kg didn't change MAP, HR and ANSR. However, in these animals Tempol 30mg/kg produced a reduction in the MAP (10 +/- 2%) without modifications in RSNA and HR. The markers of oxidative stress were significantly increased in hypertensive rats (2K1 C: 2,2 +/- 0.,4 vs C 1,6 +/- 0,3 nmol/ml, p < 0,07). In summary, we observed that in renovascular hypertension an increased in MAP and RSNA was associated with increased systemic oxidation.

CC General biology - Symposia, transactions and proceedings 00520
Pathology - Therapy 12512
Cardiovascular system - Physiology and biochemistry 14504
Cardiovascular system - Blood vessel pathology 14508
Urinary system - Pathology 15506
Pharmacology - General 22002
Pharmacology - Neuropharmacology 22024

IT Major Concepts
Pharmacology; Cardiovascular System (Transport and Circulation)

IT Diseases
renovascular hypertension: vascular disease, urologic disease, drug therapy
Hypertension, Renovascular (MeSH)

IT Chemicals & Biochemicals
tempol: neuroprotectant-drug, intravenous administration

IT Miscellaneous Descriptors
blood pressure; heart rate

ORGN Classifier
Muridae 86375
Super Taxa
Rodentia; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
rat (common): strain-Wistar, male
Taxa Notes
Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Rodents, Vertebrates

RN 2226-96-2 (tempol)

L23 ANSWER 3 OF 8 EMBASE COPYRIGHT (c) 2008 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2007234084 EMBASE
TITLE: Effects of a membrane-permeable radical scavenger, Tempol, on healing of colonic anastomoses in the cecal ligation and puncture model of polymicrobial sepsis in rats.
AUTHOR: Aytekin F.O.; Teke Z.; Aydin C.; Kabay B.; Yenisey C.; Sacar S.; Demir E.M.; Tekin K.
CORPORATE SOURCE: Dr. Z. Teke, Faculty of Medicine, Department of General Surgery, Pamukkale University, 20070 Kinikli, Denizli, Turkey. zteke_md@yahoo.com
SOURCE: American Journal of Surgery, (Jun 2007) Vol. 193, No. 6, pp. 723-729.
Refs: 46
ISSN: 0002-9610 CODEN: AJSUAB
PUBLISHER IDENT.: S 0002-9610(06)00669-6
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 030 Clinical and Experimental Pharmacology
037 Drug Literature Index
005 General Pathology and Pathological Anatomy
009 Surgery
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 15 Jun 2007
Last Updated on STN: 15 Jun 2007

AN 2007234084 EMBASE
TI Effects of a membrane-permeable radical scavenger, Tempol, on healing of colonic anastomoses in the cecal ligation and puncture model of polymicrobial sepsis in rats.
AU Aytekin F.O.; Teke Z.; Aydin C.; Kabay B.; Yenisey C.; Sacar S.; Demir E.M.; Tekin K.
CS Dr. Z. Teke, Faculty of Medicine, Department of General Surgery, Pamukkale University, 20070 Kinikli, Denizli, Turkey. zteke_md@yahoo.com
SO American Journal of Surgery, (Jun 2007) Vol. 193, No. 6, pp. 723-729.
Refs: 46
ISSN: 0002-9610 CODEN: AJSUAB
PUI S 0002-9610(06)00669-6
CY United States
DT Journal; Article
FS 030 Clinical and Experimental Pharmacology
037 Drug Literature Index
005 General Pathology and Pathological Anatomy
009 Surgery
LA English
SL English
ED Entered STN: 15 Jun 2007
Last Updated on STN: 15 Jun 2007
AB Background: Tempol (Sigma-Aldrich, Steinheim, Germany) is a stable piperidine nitroxide of low molecular weight that permeates biologic membranes and scavenges superoxide anions in vitro. In recent animal studies, the delaying effect of intraperitoneal sepsis on the healing of colonic anastomoses has been shown. In this study we aimed to investigate the effects of Tempol on the healing of colonic anastomoses in the presence of polymicrobial sepsis. Methods: Anastomosis of the left colon was performed on the day after cecal ligation and puncture (CLP) in 30 rats that were divided into 3 groups: sham-operated control (laparotomy and cecal mobilization, group I, n = 10), CLP (group II, n = 10), Tempol-treated group (30 mg/kg intravenously before the construction of colonic anastomosis, group III, n = 10). On postoperative day 6, all

animals were killed and anastomotic bursting pressures were measured in vivo. Tissue samples were obtained for further investigation of anastomotic hydroxyproline (HP) contents, perianastomotic myeloperoxidase (MPO) activity, malondialdehyde (MDA), and glutathione (GSH) levels. Results: There was a statistically significant increase in MPO activity and MDA levels in the CLP group (group II), along with a decrease in GSH levels, anastomotic HP contents, and bursting pressure values when compared with controls (group I). However, Tempol treatment led to a statistically significant increase in anastomotic bursting pressure values, tissue HP contents, and GSH levels, along with a decrease in MPO activity and MDA levels in group III ($P < .05$). Conclusions: This study showed that Tempol treatment significantly prevented the delaying effect of CLP-induced polymicrobial sepsis on anastomotic healing in the left colon. Further clinical studies are needed to clarify whether Tempol may be a useful therapeutic agent to increase the safety of the anastomosis during particular surgeries in which sepsis-induced organ injury occurs.

CT Medical Descriptors:
animal experiment
animal model
animal tissue
article
body weight
cecum
*colon anastomosis
controlled study
drug mechanism
drug penetration
enzyme activity
in vivo study
infection prevention
intestine motility
*laparotomy
ligation
male
membrane permeability
nonhuman
postoperative period
pressure measurement
priority journal
puncture
rat
*sepsis: DT, drug therapy
*sepsis: PC, prevention
single drug dose
*wound healing

CT Drug Descriptors:
ciprofloxacin: CB, drug combination
ciprofloxacin: DT, drug therapy
clindamycin: CB, drug combination
clindamycin: DT, drug therapy
glutathione: EC, endogenous compound
hydroxyproline
malonaldehyde: EC, endogenous compound
myeloperoxidase: EC, endogenous compound
*scavenger: PK, pharmacokinetics
*scavenger: PD, pharmacology
*tempol: IV, intravenous drug administration
*tempol: PK, pharmacokinetics
*tempol: PD, pharmacology

RN (ciprofloxacin) 85721-33-1; (clindamycin) 18323-44-9; (glutathione)

70-18-8; (hydroxyproline) 51-35-4, 6912-67-0; (malonaldehyde) 542-78-9; (tempol) 2226-96-2
CO Sigma Aldrich (Germany)

L23 ANSWER 4 OF 8 EMBASE COPYRIGHT (c) 2008 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2005263585 EMBASE
TITLE: Medical treatment of radiological casualties: Current concepts.
AUTHOR: Koenig K.L.; Goans R.E.; Hatchett R.J.; Mettler Jr. F.A.; Schumacher T.A.; Noji E.K.; Jarrett D.G.
CORPORATE SOURCE: Dr. R.E. Goans, Occupational and Radiation Medicine, MJW Corporation, 1422 Eagle Bend Drive, Clinton, TN 37716, United States. ronald.goans@comcast.net
SOURCE: Annals of Emergency Medicine, (Jun 2005) Vol. 45, No. 6, pp. 643-652.
Refs: 29
ISSN: 0196-0644 CODEN: AEMED3
PUBLISHER IDENT.: S 0196-0644(05)00086-7
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 014 Radiology
017 Public Health, Social Medicine and Epidemiology
024 Anesthesiology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 7 Jul 2005
Last Updated on STN: 7 Jul 2005
AN 2005263585 EMBASE
TI Medical treatment of radiological casualties: Current concepts.
AU Koenig K.L.; Goans R.E.; Hatchett R.J.; Mettler Jr. F.A.; Schumacher T.A.; Noji E.K.; Jarrett D.G.
CS Dr. R.E. Goans, Occupational and Radiation Medicine, MJW Corporation, 1422 Eagle Bend Drive, Clinton, TN 37716, United States. ronald.goans@comcast.net
SO Annals of Emergency Medicine, (Jun 2005) Vol. 45, No. 6, pp. 643-652.
Refs: 29
ISSN: 0196-0644 CODEN: AEMED3
PUI S 0196-0644(05)00086-7
CY United States
DT Journal; General Review; (Review)
FS 014 Radiology
017 Public Health, Social Medicine and Epidemiology
024 Anesthesiology
037 Drug Literature Index
038 Adverse Reactions Titles
LA English
SL English
ED Entered STN: 7 Jul 2005
Last Updated on STN: 7 Jul 2005
AB The threat of radiologic or nuclear terrorism is increasing, yet many physicians are unfamiliar with basic treatment principles for radiologic casualties. Patients may present for care after a covert radiation exposure, requiring an elevated level of suspicion by the physician. Traditional medical and surgical triage criteria should always take precedence over radiation exposure management or decontamination. External contamination from a radioactive cloud is easily evaluated using a simple Geiger-Muller counter and decontamination accomplished by prompt removal of clothing and traditional showering. Management of surgical

conditions in the presence of persistent radioactive contamination should be dealt with in a conventional manner with health physics guidance. To be most effective in the medical management of a terrorist event involving high-level radiation, physicians should understand basic manifestations of the acute radiation syndrome, the available medical countermeasures, and the psychosocial implications of radiation incidents. Health policy considerations include stockpiling strategies, effective use of risk communications, and decisionmaking for shelter-in-place versus evacuation after a radiologic incident.

CT Medical Descriptors:
bone marrow transplantation
clothing
constipation: SI, side effect
decision making
disease severity
drug eruption: SI, side effect
drug hypersensitivity: SI, side effect
gastrointestinal symptom: SI, side effect
health care policy
health physics
human
hypocalcemia: SI, side effect
hypotension: SI, side effect
infection complication: CO, complication
infection complication: DT, drug therapy
infection complication: PC, prevention
infection prevention
intoxication: DT, drug therapy
lactate strontium: DT, drug therapy
nausea and vomiting: SI, side effect
neutropenia: DT, drug therapy
patient care
physician
  plastic surgery
priority journal
prognosis
psychological aspect
radiation dose
radiation exposure
*radiation injury: DT, drug therapy
*radiation injury: ET, etiology
*radiation injury: PC, prevention
  *radiation injury: SU, surgery
*radiation injury: TH, therapy
radiation protection
radioactive contamination
review
stem cell transplantation
symptomatology
thyroid disease: SI, side effect
whole body radiation

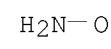
CT Drug Descriptors:
alginic acid
aluminum hydroxide
aluminum phosphate: DT, drug therapy
amifostine: AE, adverse drug reaction
amifostine: DT, drug therapy
  amifostine: IV, intravenous drug administration
aminothiol
ammonium chloride: DT, drug therapy

androstenediol
antacid agent: DT, drug therapy
antibiotic agent: DT, drug therapy
antithyroid agent: DT, drug therapy
barium sulfate
bicarbonate
captopril
charcoal: DT, drug therapy
colony stimulating factor: EC, endogenous compound
dipeptidyl carboxypeptidase inhibitor
emetic agent: DT, drug therapy
ferric ferrocyanide: AE, adverse drug reaction
ferric ferrocyanide: DT, drug therapy
ferric ferrocyanide: PO, oral drug administration
ferric ferrocyanide: PD, pharmacology
genistein
gluconate calcium
glutamine
keratinocyte growth factor
lactic acid derivative: DT, drug therapy
laxative: DT, drug therapy
magnesium carbonate
nitroxide
parathyroid extract: DT, drug therapy
penicillin G
pentetate calcium: DO, drug dose
pentetate calcium: DT, drug therapy
  pentetate calcium: IV, intravenous drug administration
pentetate zinc: DO, drug dose
pentetate zinc: DT, drug therapy
  pentetate zinc: IV, intravenous drug administration
pentoxifylline
phosphate: DT, drug therapy
phosphate: PO, oral drug administration
phosphonol
potassium iodide: AE, adverse drug reaction
potassium iodide: DT, drug therapy
recombinant colony stimulating factor: DT, drug therapy
recombinant colony stimulating factor: SC, subcutaneous drug administration
recombinant granulocyte colony stimulating factor: DT, drug therapy
recombinant granulocyte colony stimulating factor: SC, subcutaneous drug administration
recombinant granulocyte macrophage colony stimulating factor: DT, drug therapy
recombinant granulocyte macrophage colony stimulating factor: SC, subcutaneous drug administration
tempol
unclassified drug
vasodilator agent: DT, drug therapy

RN (alginic acid) 28961-37-7, 29894-36-8, 9005-32-7, 9005-38-3; (aluminum hydroxide) 1330-44-5, 20257-20-9, 21645-51-2, 80206-84-4; (aluminum phosphate) 7784-30-7; (amifostine) 20537-88-6; (ammonium chloride) 12125-02-9; (androstenediol) 28652-91-7, 521-17-5; (barium sulfate) 13462-86-7, 7727-43-7, 8057-67-8; (bicarbonate) 144-55-8, 71-52-3; (captopril) 62571-86-2; (charcoal) 16291-96-6; (colony stimulating factor) 62683-29-8; (ferric ferrocyanide) 12240-15-2, 14038-43-8, 14433-93-3, 14460-02-7; (genistein) 446-72-0; (gluconate calcium) 299-28-5; (glutamine) 56-85-9, 6899-04-3; (keratinocyte growth factor) 126469-10-1; (magnesium carbonate) 546-93-0; (nitroxide) 13408-29-2; (penicillin G) 1406-05-9, 61-33-6; (pentetate calcium) 2531-75-1;

(pentetate zinc) 23759-24-2; (pentoxifylline) 6493-05-6; (phosphate) 14066-19-4, 14265-44-2; (potassium iodide) 7681-11-0; (recombinant granulocyte colony stimulating factor) 121181-53-1; (recombinant granulocyte macrophage colony stimulating factor) 99283-10-0; (tempol) 2226-96-2

L23 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2008 ACS on STN
IT 13408-29-2, Nitroxide
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of furoxan compds. as non-thrombogenic materials)
RN 13408-29-2 CAPLUS
CN Nitroxide (7CI, 8CI, 9CI) (CA INDEX NAME)



ACCESSION NUMBER: 2007:561735 CAPLUS
DOCUMENT NUMBER: 147:9920
TITLE: Furoxan compounds as non-thrombogenic materials, their preparation, pharmaceutical compositions, and use in therapy
INVENTOR(S): Garvey, David S.; Ranatunge, Ramani R.
PATENT ASSIGNEE(S): Nitromed, Inc., USA
SOURCE: PCT Int. Appl., 76pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007059311	A2	20070524	WO 2006-US44680	20061116
WO 2007059311	A3	20071221		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

PRIORITY APPLN. INFO.: US 2005-736871P P 20051116
OTHER SOURCE(S): MARPAT 147:9920
AN 2007:561735 CAPLUS
DN 147:9920
ED Entered STN: 24 May 2007
TI Furoxan compounds as non-thrombogenic materials, their preparation, pharmaceutical compositions, and use in therapy
IN Garvey, David S.; Ranatunge, Ramani R.
PA Nitromed, Inc., USA
SO PCT Int. Appl., 76pp.
CODEN: PIXXD2
DT Patent
LA English

CC 28-10 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 63

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2007059311	A2	20070524	WO 2006-US44680	20061116
	WO 2007059311	A3	20071221		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

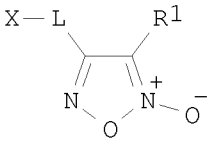
PRAI US 2005-736871P P 20051116

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2007059311	IPCI	A61K0031-445 [I,A]; C07D0271-00 [I,C]; C07D0271-12 [I,A]
	IPCR	C07D0271-00 [I,C]; C07D0271-12 [I,A]

OS MARPAT 147:9920

GI



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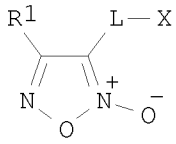
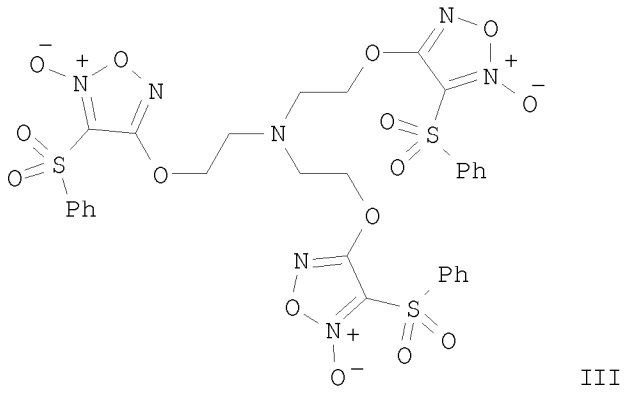


II



III

AB The invention relates to furoxan compds. of formula I or II, which inhibit platelet deposition and thrombus formation on artificial surfaces. In compds. I and II, R1 is selected from cyano, nitro, (un)substituted Ph, (un)substituted phenylsulfonyl, (un)substituted carbamoyl, alkoxycarbonyl,

and aryloxycarbonyl; L is a bond, O, S(O)p, or NR2, where p is 0-2 and R2 is H, lower alkyl, or aryl; X is -(CH2)a-NR3R4, -(CHR5)b-CH2-L-Z, -(CHR5)b-NR3R4, or -CH2-C(CH2-L-Z)3; a is 2-5; b is 1-6; R3 is H, alkyl, aryl, or -(CH2)a-L-Z; R4 is H, alkyl, aryl, -(CH2)a-L-Z, or -C(CH2-L-Z)3; R5 is H, or -L-Z; and Z is R1-substituted furoxan; provided that compds. I and II must contain at least one Z group; including pharmaceutically acceptable salts thereof. The invention also relates to the preparation of I and II, pharmaceutical compns. comprising a compound I or II and a pharmaceutically acceptable carrier, as well as to the use of the compns. for treating cardiovascular diseases and for preventing adverse consequences resulting from the interaction between blood and artificial surfaces, such as on medical devices. Oxidation of (phenylthio)acetic acid followed by dimerization with nitric acid and substitution with triethanolamine gave furoxan III. The compds. of the invention inhibit the proliferation of vascular smooth muscle and endothelial cells, e.g., the citrate salt of compound III expressed IC50 values of 6 nM and 447 nM, resp.

ST furoxan prepn cardiovascular agent; platelet aggregation inhibitor furoxan prepn

IT Oxidative stress, biological
(-associated diseases; preparation of furoxan compds. as non-thrombogenic materials)

IT Thiols, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(S-nitro-, codrugs; preparation of furoxan compds. as non-thrombogenic materials)

IT Thiols, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(S-nitroso, codrugs; preparation of furoxan compds. as non-thrombogenic materials)

IT Platelet (blood)
(adhesion; preparation of furoxan compds. as non-thrombogenic materials)

IT Antiarteriosclerotics
(antiatherosclerotics; preparation of furoxan compds. as non-thrombogenic materials)

IT Hyperplasia
(arterial intimal; preparation of furoxan compds. as non-thrombogenic materials)

IT Blood vessel
(arteriovenous anastomosis; preparation of furoxan compds. as non-thrombogenic materials)

IT Blood vessel
(artificial; preparation of furoxan compds. as non-thrombogenic materials)

IT Medical goods
(balloons; preparation of furoxan compds. as non-thrombogenic materials)

IT Transplant and Transplantation
(blood vessel, synthetic; preparation of furoxan compds. as non-thrombogenic materials)

IT Transplant and Transplantation
(blood vessel; preparation of furoxan compds. as non-thrombogenic materials)

IT Medical goods
(brain stimulator; preparation of furoxan compds. as non-thrombogenic materials)

IT Medical goods
(cardioverter defibrillator; preparation of furoxan compds. as non-thrombogenic materials)

IT Drug delivery systems
(catheter for; preparation of furoxan compds. as non-thrombogenic materials)

IT Medical goods

(catheters, catheter tip; preparation of furoxan compds. as non-thrombogenic materials)
IT Medical goods
(catheters; preparation of furoxan compds. as non-thrombogenic materials)
IT Embolism
(cerebral thromboembolism; preparation of furoxan compds. as non-thrombogenic materials)
IT Ischemia
(cerebral; preparation of furoxan compds. as non-thrombogenic materials)
IT Brain, disease
(cerebrovascular; preparation of furoxan compds. as non-thrombogenic materials)
IT Medical goods
(chemical sensor; preparation of furoxan compds. as non-thrombogenic materials)
IT Angiotensin receptor antagonists
Antidiabetic agents
Antioxidants
Calcium channel blockers
Endothelin receptor antagonists
H2-antihistamines
Hypolipemic agents
Immunosuppressants
Potassium channel blockers
Radiotherapy
Vasodilators
α-Adrenoceptor antagonists
β-Adrenoceptor antagonists
(codrugs; preparation of furoxan compds. as non-thrombogenic materials)
IT Heavy metals
RL: DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrugs; preparation of furoxan compds. as non-thrombogenic materials)
IT Nitrosamines
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrugs; preparation of furoxan compds. as non-thrombogenic materials)
IT Oximes
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrugs; preparation of furoxan compds. as non-thrombogenic materials)
IT Steroids, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrugs; preparation of furoxan compds. as non-thrombogenic materials)
IT Inflammation
(coronary plaque; preparation of furoxan compds. as non-thrombogenic materials)
IT Medical goods
(defibrillator; preparation of furoxan compds. as non-thrombogenic materials)
IT Medical goods
(dialysis bag; preparation of furoxan compds. as non-thrombogenic materials)
IT Cardiovascular system, disease
(diastolic dysfunction; preparation of furoxan compds. as non-thrombogenic materials)
IT Drug delivery systems
(drug pump; preparation of furoxan compds. as non-thrombogenic materials)
IT Blood vessel, disease
(endothelial dysfunction; preparation of furoxan compds. as non-thrombogenic materials)

IT Blood vessel
(endothelium; preparation of furoxan compds. as non-thrombogenic materials)
IT Medical goods
(implantable cardiac defibrillator; preparation of furoxan compds. as non-thrombogenic materials)
IT Medical goods
(implantable pulse generator; preparation of furoxan compds. as non-thrombogenic materials)
IT Prosthetic materials and Prosthetics
(implants, artificial heart pacemaker; preparation of furoxan compds. as non-thrombogenic materials)
IT Prosthetic materials and Prosthetics
(implants, heart valve; preparation of furoxan compds. as non-thrombogenic materials)
IT Artery, disease
(intima, hyperplasia; preparation of furoxan compds. as non-thrombogenic materials)
IT Brain, disease
(ischemia; preparation of furoxan compds. as non-thrombogenic materials)
IT Medical goods
(lead; preparation of furoxan compds. as non-thrombogenic materials)
IT Heart, disease
(left ventricle; preparation of furoxan compds. as non-thrombogenic materials)
IT Ventricular hypertrophy
(left; preparation of furoxan compds. as non-thrombogenic materials)
IT Wound
(medical device use-associated; preparation of furoxan compds. as non-thrombogenic materials)
IT Medical goods
(membrane surface; preparation of furoxan compds. as non-thrombogenic materials)
IT Infection
(microbial; preparation of furoxan compds. as non-thrombogenic materials)
IT Angioplasty
(neointimal hyperplasia following; preparation of furoxan compds. as non-thrombogenic materials)
IT Artery, disease
(occlusion, thrombotic; preparation of furoxan compds. as non-thrombogenic materials)
IT Heart
(pacemaker, artificial; preparation of furoxan compds. as non-thrombogenic materials)
IT Blood vessel, disease
(peripheral; preparation of furoxan compds. as non-thrombogenic materials)
IT Adhesion, biological
(platelet; preparation of furoxan compds. as non-thrombogenic materials)
IT Myocardial infarction
(post-; preparation of furoxan compds. as non-thrombogenic materials)
IT Vascular restenosis
(post-angioplasty; preparation of furoxan compds. as non-thrombogenic materials)
IT Aneurysm
Angina pectoris
Anti-inflammatory agents
Anti-ischemic agents
Antianginal agents
Antiarrhythmics
Anticholesteremic agents
Anticoagulants

Antihypertensives
Antimicrobial agents
Antitumor agents
Atherosclerosis
Atrial fibrillation
Atrial flutter
Autoimmune disease
Blood
Blood vessel, disease
Brain infarction
Cardiac arrhythmia
Cardiovascular agents
Cardiovascular system, disease
Combination chemotherapy
Coronary artery disease
Coronary bypass surgery
Coronary restenosis
Cytotoxic agents
Diabetes mellitus
Embolism
Heart failure
Human
Hypercholesterolemia
Hypertension
Immunomodulators
Immunosuppressants
Inflammation
Medical goods
Myocardial infarction
Myocardial ischemia
Nonsteroidal anti-inflammatory drugs
Pharmaceutical carriers
Platelet aggregation inhibitors
Shock (circulatory collapse)
Thrombolytics
Thrombosis
Transplant rejection
Vascular restenosis
Vascular smooth muscle
Wound healing
Wound healing promoters
(preparation of furoxan compds. as non-thrombogenic materials)

IT Mineralocorticoid receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation of furoxan compds. as non-thrombogenic materials)

IT Disease, animal
(proliferative, hyper-; preparation of furoxan compds. as non-thrombogenic materials)

IT Disease, animal
(proliferative; preparation of furoxan compds. as non-thrombogenic materials)

IT Transport proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(proton pump, inhibitors, codrugs; preparation of furoxan compds. as non-thrombogenic materials)

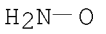
IT Imaging agents
(radiog. contrast agents; preparation of furoxan compds. as non-thrombogenic materials)

IT Platelet (blood)
(reducing agent, codrugs; preparation of furoxan compds. as non-thrombogenic materials)

IT Medical goods
(sacral nerve stimulator; preparation of furoxan compds. as non-thrombogenic materials)
IT Cell proliferation
(smooth muscle; preparation of furoxan compds. as non-thrombogenic materials)
IT Medical goods
(spinal stimulator; preparation of furoxan compds. as non-thrombogenic materials)
IT Medical goods
(stents; preparation of furoxan compds. as non-thrombogenic materials)
IT Artery, disease
(stiffness; preparation of furoxan compds. as non-thrombogenic materials)
IT Brain, disease
(stroke; preparation of furoxan compds. as non-thrombogenic materials)
IT Medical goods
(sutures; preparation of furoxan compds. as non-thrombogenic materials)
IT Embolism
(thromboembolism; preparation of furoxan compds. as non-thrombogenic materials)
IT Blood vessel
(transplant, synthetic; preparation of furoxan compds. as non-thrombogenic materials)
IT Blood vessel
(transplant; preparation of furoxan compds. as non-thrombogenic materials)
IT Medical goods
(tubes; preparation of furoxan compds. as non-thrombogenic materials)
IT Medical goods
(use-associated vascular or non-vascular complications; preparation of furoxan
compds. as non-thrombogenic materials)
IT Heart
(valve, artificial; preparation of furoxan compds. as non-thrombogenic materials)
IT Endothelium
(vascular, disease; preparation of furoxan compds. as non-thrombogenic materials)
IT Endothelium
(vascular; preparation of furoxan compds. as non-thrombogenic materials)
IT Blood vessel
(wall injury; preparation of furoxan compds. as non-thrombogenic materials)
IT Wound healing
(wound contraction inhibitors; preparation of furoxan compds. as non-thrombogenic materials)
IT 937274-19-6P
RL: BYP (Byproduct); PREP (Preparation)
(byproduct; preparation of furoxan compds. as non-thrombogenic materials)
IT 112-05-0, Nonoic acid 127-07-1, Hydroxyurea 497-27-8, Furoxan
7803-49-8, Hydroxylamine, biological studies 13115-21-4,
N-Hydroxyguanidine 13408-29-2, Nitroxide 14448-38-5,
Hyponitrous acid 29909-71-5, 1,2,3,4-Oxatriazol-5-amine 35576-91-1,
Nitrosamide
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of furoxan compds. as non-thrombogenic materials)
IT 937274-07-2P 937274-12-9P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(drug candidate; preparation of furoxan compds. as non-thrombogenic materials)

IT 937274-08-3P 937274-13-0P 937274-15-2P 937274-16-3P 937274-17-4P
937274-18-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of furoxan compds. as non-thrombogenic materials)
IT 9015-82-1 9040-59-9, Cyclic nucleotide phosphodiesterase 82707-54-8, Neutral endopeptidase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors, codrugs; preparation of furoxan compds. as non-thrombogenic materials)
IT 3959-23-7P, (Phenylsulfonyl)acetic acid 66074-00-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of furoxan compds. as non-thrombogenic materials)
IT 9015-94-5, Renin, biological studies 10102-43-9, Nitric oxide, biological studies 329900-75-6, Cyclooxygenase-2
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation of furoxan compds. as non-thrombogenic materials)
IT 86-54-4D, Hydralazine, compds. 14797-55-8, Nitrate, biological studies 14797-65-0, Nitrite, biological studies 20273-10-3, Sydnonimine 57842-39-4
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of furoxan compds. as non-thrombogenic materials)
IT 56-81-5, Glycerol, reactions 102-71-6, Triethanolamine, reactions 103-04-8, (Phenylthio)acetic acid 111-42-2, Diethanolamine, reactions 220270-86-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(starting material; preparation of furoxan compds. as non-thrombogenic materials)

L23 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2008 ACS on STN
IT 13408-29-2, Nitroxide
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of benzimidazole-tetrazole-nitric oxide compds. as enhancing angiotensin II antagonist compds. and their use in treatment of disease)
RN 13408-29-2 CAPLUS
CN Nitroxide (7CI, 8CI, 9CI) (CA INDEX NAME)



ACCESSION NUMBER: 2007:146833 CAPLUS
DOCUMENT NUMBER: 146:229356
TITLE: Nitric oxide enhancing angiotensin II antagonist compounds, and their preparation, compositions, and methods of use
INVENTOR(S): Garvey, David S.; Cai, Xiong; Fang, Xinqin; Ranatunge, Ramani R.; Wey, Shiow-Jyi; Zhai, Hai-Xiao
PATENT ASSIGNEE(S): Nitromed, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 58pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
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PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2007032533	A1	20070208	US 2006-499770	20060807
WO 2007019448	A2	20070215	WO 2006-US30733	20060807

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.:	US 2005-706005P	P	20050808
	US 2005-706419P	P	20050809
	US 2005-748579P	P	20051209

OTHER SOURCE(S): MARPAT 146:229356

AN 2007:146833 CAPLUS

DN 146:229356

ED Entered STN: 09 Feb 2007

TI Nitric oxide enhancing angiotensin II antagonist compounds, and their preparation, compositions, and methods of use

IN Garvey, David S.; Cai, Xiong; Fang, Xinqin; Ranatunge, Ramani R.; Wey, Shiow-Jyi; Zhai, Hai-Xiao

PA Nitromed, Inc., USA

SO U.S. Pat. Appl. Publ., 58pp.
CODEN: USXXCO

DT Patent

LA English

INCL 514362000; 514364000; 514378000; 514381000; 548125000; 548143000; 548253000

CC 28-10 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 63

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2007032533	A1	20070208	US 2006-499770	20060807
	WO 2007019448	A2	20070215	WO 2006-US30733	20060807

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRAI	US 2005-706005P	P	20050808
	US 2005-706419P	P	20050809
	US 2005-748579P	P	20051209

CLASS

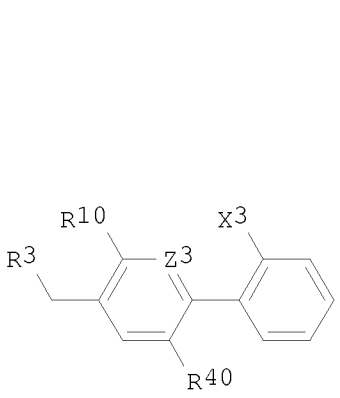
PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
US 2007032533	INCL	514362000; 514364000; 514378000; 514381000; 548125000;

548143000; 548253000
IPCI A61K0031-433 [I,A]; A61K0031-4245 [I,A]; A61K0031-42 [I,A]
IPCR A61K0031-433 [I,C]; A61K0031-433 [I,A]; A61K0031-42 [I,C]; A61K0031-42 [I,A]; A61K0031-4245 [I,C]; A61K0031-4245 [I,A]
NCL 514/362.000; 514/364.000; 514/378.000; 514/381.000; 548/125.000; 548/143.000; 548/253.000

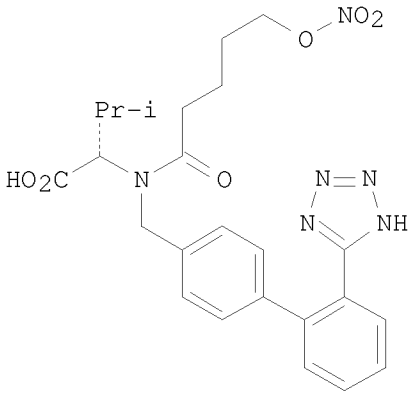
WO 2007019448 IPCI A61K0031-4245 [I,A]; A61K0031-433 [I,A]; A61K0031-42 [I,A]
IPCR A61K0031-4245 [I,C]; A61K0031-4245 [I,A]; A61K0031-42 [I,C]; A61K0031-42 [I,A]; A61K0031-433 [I,C]; A61K0031-433 [I,A]

OS MARPAT 146:229356

GI



I



II

AB The invention describes compns. and kits comprising at least one nitric oxide enhancing angiotensin II antagonist compound of formula I, or pharmaceutically acceptable salts thereof, and compns. comprising at least one nitric oxide enhancing angiotensin II antagonist compound, and, optionally, at least one nitric oxide enhancing compound and/or at least one therapeutic agent. Compds. of formula I wherein X3 is (un)substituted azole, (un)substituted sulfonylaminoxazole, (un)substituted aminosulfonyl, (un)substituted acyl, etc.; Y3 is (un)substituted azole, (un)substitute valine derivative, (un)substituted amide, etc.; Z3 is CH and N; R10 is F and H; R40 is H, lower alkyl, alkoxyalkyl, etc.; and their pharmaceutically acceptable salts thereof are claimed. The invention also provides methods for (a) treating cardiovascular diseases; (b) treating renovascular diseases; (c) treating diabetes; (d) treating diseases resulting from oxidative stress; (e) treating endothelial dysfunctions; (f) treating diseases caused by endothelial dysfunctions; (g) treating cirrhosis; (h) treating pre-eclampsia; (j) treating osteoporosis; (k) treating nephropathy; (l) treating peripheral vascular diseases; (m) treating portal hypertension (o) treating central nervous system disorders; (p) treating metabolic syndrome; and (q) treating hyperlipidemia. The nitric oxide enhancing angiotensin II antagonist compds. comprise at least one nitric oxide enhancing group linked to the angiotensin II antagonist compound through one or more sites such as carbon, oxygen and/or nitrogen via a bond or moiety that cannot be hydrolyzed. Example compound II was prepared by reduction of 2'[2-(1-methyl-1-phenylethyl)-2H-tetrazol-5-yl]-[1,1'-biphenyl]-4-carboxylic acid Me ester; the resulting 2'[2-(1-methyl-1-phenylethyl)-2H-tetrazol-5-yl]-[1,1'-biphenyl]-4-methanol underwent oxidation to give 2'[2-(1-methyl-1-phenylethyl)-2H-tetrazol-5-yl]-[1,1'-biphenyl]-4-

carboxaldehyde, which underwent condensation with L-valine tert-Bu ester hydrochloride to give (E)-N-[2'[2-(1-methyl-1-phenylethyl)-2H-tetrazol-5-yl]-[1,1'-biphenyl]-4-methylene]-L-valine tert-Bu ester, which underwent reduction to give N-[2'[2-(1-methyl-1-phenylethyl)-2H-tetrazol-5-yl]-[1,1'-biphenyl]-4-methyl]-L-valine tert-Bu ester, which underwent amidation with 5-(nitrooxy)pentanoic acid to give N-[2'[2-(1-methyl-1-phenylethyl)-2H-tetrazol-5-yl]-[1,1'-biphenyl]-4-methyl]-N-[5-(nitrooxy)-1-oxopentyl]-L-valine tert-Bu ester, which underwent hydrolysis to give N-[2'[2-(1-methyl-1-phenylethyl)-2H-tetrazol-5-yl]-[1,1'-biphenyl]-4-methyl]-N-[5-(nitrooxy)-1-oxopentyl]-L-valine, which underwent detritylation to give compound II. All the invention compds. were evaluated for their AT1 inhibitory activity. From the assay, it was determined that compound II exhibited an IC50 value of 19 nM and 86% inhibition at 100 nM.

ST benzimidazole tetrazole nitric oxide prepn angiotensin II antagonist

IT Platelet (blood)
(-reducing agents, codrugs; preparation of benzimidazole-tetrazole-nitric oxide compds. as enhancing angiotensin II antagonist compds. and their use in treatment of disease)

IT Thiols, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(S-nitro-, codrugs; preparation of benzimidazole-tetrazole-nitric oxide compds. as enhancing angiotensin II antagonist compds. and their use in treatment of disease)

IT Thiols, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(S-nitroso, codrugs; preparation of benzimidazole-tetrazole-nitric oxide compds. as enhancing angiotensin II antagonist compds. and their use in treatment of disease)

IT Antiarteriosclerotics
(antiatherosclerotics; preparation of benzimidazole-tetrazole-nitric oxide compds. as enhancing angiotensin II antagonist compds. and their use in treatment of disease)

IT Hyperplasia
(arterial intimal, following percutaneous transluminal coronary angiog., treatment of; preparation of benzimidazole-tetrazole-nitric oxide compds. as enhancing angiotensin II antagonist compds. and their use in treatment of disease)

IT Blood vessel
(artificial; preparation of benzimidazole-tetrazole-nitric oxide compds. as enhancing angiotensin II antagonist compds. and their use in treatment of disease)

IT Embolism
(cerebral thromboembolism, treatment of; preparation of benzimidazole-tetrazole-nitric oxide compds. as enhancing angiotensin II antagonist compds. and their use in treatment of disease)

IT Ischemia
(cerebral, treatment of; preparation of benzimidazole-tetrazole-nitric oxide compds. as enhancing angiotensin II antagonist compds. and their use in treatment of disease)

IT Brain, disease
(cerebrovascular, thrombotic occlusion and reclusion, treatment of; preparation of benzimidazole-tetrazole-nitric oxide compds. as enhancing angiotensin II antagonist compds. and their use in treatment of disease)

IT Brain, disease
(cerebrovascular, treatment of; preparation of benzimidazole-tetrazole-nitric oxide compds. as enhancing angiotensin II antagonist compds. and their use in treatment of disease)

IT Angiotensin receptor antagonists

Anticoagulants
Antidiabetic agents
Antioxidants
Calcium channel blockers
Digitalis purpurea
Diuretics
Endothelin receptor antagonists
H2-antihistamines
Nonsteroidal anti-inflammatory drugs
Potassium channel blockers
Vasodilators
α-Adrenoceptor antagonists
β-Adrenoceptor antagonists
(codrugs; preparation of benzimidazole-tetrazole-nitric oxide compds. as enhancing angiotensin II antagonist compds. and their use in treatment of disease)

IT Angiotensin AT1 receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(codrugs; preparation of benzimidazole-tetrazole-nitric oxide compds. as enhancing angiotensin II antagonist compds. and their use in treatment of disease)

IT Oximes
Prostaglandins
Steroids, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrugs; preparation of benzimidazole-tetrazole-nitric oxide compds. as enhancing angiotensin II antagonist compds. and their use in treatment of disease)

IT Inflammation
(coronary plaque, treatment of; preparation of benzimidazole-tetrazole-nitric oxide compds. as enhancing angiotensin II antagonist compds. and their use in treatment of disease)

IT Cardiovascular system, disease
(diastolic dysfunction, treatment of; preparation of benzimidazole-tetrazole-nitric oxide compds. as enhancing angiotensin II antagonist compds. and their use in treatment of disease)

IT Blood vessel, disease
(endothelial dysfunction, -induced diseases, treatment of; preparation of benzimidazole-tetrazole-nitric oxide compds. as enhancing angiotensin II antagonist compds. and their use in treatment of disease)

IT Blood vessel, disease
(endothelial dysfunction, treatment of; preparation of benzimidazole-tetrazole-nitric oxide compds. as enhancing angiotensin II antagonist compds. and their use in treatment of disease)

IT Kidney, disease
(failure, treatment of; preparation of benzimidazole-tetrazole-nitric oxide compds. as enhancing angiotensin II antagonist compds. and their use in treatment of disease)

IT Artery, disease
(intima, hyperplasia, following percutaneous transluminal coronary angiog., treatment of; preparation of benzimidazole-tetrazole-nitric oxide compds. as enhancing angiotensin II antagonist compds. and their use in treatment of disease)

IT Brain, disease
(ischemia, treatment of; preparation of benzimidazole-tetrazole-nitric oxide compds. as enhancing angiotensin II antagonist compds. and their use in treatment of disease)

IT Heart, disease
(left ventricle, treatment of; preparation of benzimidazole-tetrazole-nitric

oxide compds. as enhancing angiotensin II antagonist compds. and their use in treatment of disease)

IT Ventricular hypertrophy
(left, treatment of; preparation of benzimidazole-tetrazole-nitric oxide compds. as enhancing angiotensin II antagonist compds. and their use in treatment of disease)

IT Blood vessel, disease
Wound
(medical device-associated, treatment of; preparation of benzimidazole-tetrazole-nitric oxide compds. as enhancing angiotensin II antagonist compds. and their use in treatment of disease)

IT Metabolic disorders
(metabolic syndrome X, treatment of; preparation of benzimidazole-tetrazole-nitric oxide compds. as enhancing angiotensin II antagonist compds. and their use in treatment of disease)

IT Coronary angioplasty
(neointimal hyperplasia following, treatment of; preparation of benzimidazole-tetrazole-nitric oxide compds. as enhancing angiotensin II antagonist compds. and their use in treatment of disease)

IT Blood vessel, disease
(peripheral, treatment of; preparation of benzimidazole-tetrazole-nitric oxide compds. as enhancing angiotensin II antagonist compds. and their use in treatment of disease)

IT Adhesion, biological
(platelet; preparation of benzimidazole-tetrazole-nitric oxide compds. as enhancing angiotensin II antagonist compds. and their use in treatment of disease)

IT Hypertension
(portal, treatment of; preparation of benzimidazole-tetrazole-nitric oxide compds. as enhancing angiotensin II antagonist compds. and their use in treatment of disease)

IT Angioplasty
(post-, restenosis, treatment of; preparation of benzimidazole-tetrazole-nitric oxide compds. as enhancing angiotensin II antagonist compds. and their use in treatment of disease)

IT Anti-inflammatory agents
Anti-ischemic agents
Antianginal agents
Antiarrhythmics
Anticholesteremic agents
Antihypertensives
Antiosteoporotic agents
Cardiovascular agents
Combination chemotherapy
Coronary bypass surgery
Cytotoxic agents
Human
Hypolipemic agents
Immunosuppressants
Pharmaceutical carriers
Platelet aggregation
Platelet aggregation inhibitors
Thrombolytics
Wound healing promoters
(preparation of benzimidazole-tetrazole-nitric oxide compds. as enhancing angiotensin II antagonist compds. and their use in treatment of disease)

IT α-Adrenoceptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation of benzimidazole-tetrazole-nitric oxide compds. as enhancing angiotensin II antagonist compds. and their use in treatment of

disease)
IT Transport proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(proton pump, inhibitors, codrugs; preparation of benzimidazole-tetrazole-nitric oxide compds. as enhancing angiotensin II antagonist compds. and their use in treatment of disease)
IT Hypertension
(renal, renal deterioration associated with, treatment of; preparation of benzimidazole-tetrazole-nitric oxide compds. as enhancing angiotensin II antagonist compds. and their use in treatment of disease)
IT Blood vessel, disease
(reno-, treatment of; preparation of benzimidazole-tetrazole-nitric oxide compds. as enhancing angiotensin II antagonist compds. and their use in treatment of disease)
IT Hypertension
(severe, renal deterioration associated with, treatment of; preparation of benzimidazole-tetrazole-nitric oxide compds. as enhancing angiotensin II antagonist compds. and their use in treatment of disease)
IT Cell proliferation
(smooth muscle; preparation of benzimidazole-tetrazole-nitric oxide compds. as enhancing angiotensin II antagonist compds. and their use in treatment of disease)
IT Artery, disease
(stiffness, treatment of; preparation of benzimidazole-tetrazole-nitric oxide compds. as enhancing angiotensin II antagonist compds. and their use in treatment of disease)
IT Brain, disease
(stroke, treatment of; preparation of benzimidazole-tetrazole-nitric oxide compds. as enhancing angiotensin II antagonist compds. and their use in treatment of disease)
IT Embolism
(thromboembolism, treatment of; preparation of benzimidazole-tetrazole-nitric oxide compds. as enhancing angiotensin II antagonist compds. and their use in treatment of disease)
IT Aneurysm
Angina pectoris
Atherosclerosis
Atrial fibrillation
Atrial flutter
Brain infarction
Cardiac arrhythmia
Cardiovascular system, disease
Cirrhosis
Coronary artery disease
Coronary restenosis
Diabetes mellitus
Embolism
Eye, disease
Heart failure
Hypercholesterolemia
Hyperlipidemia
Hypertension
Kidney, disease
Myocardial infarction
Myocardial ischemia
Osteoporosis
Oxidative stress, biological
Preeclampsia
Shock (circulatory collapse)
Thrombosis
Vascular restenosis

Wound healing
(treatment of; preparation of benzimidazole-tetrazole-nitric oxide compds. as enhancing angiotensin II antagonist compds. and their use in treatment of disease)

IT Medical goods
(vascular or non-vascular complications associated with; preparation of benzimidazole-tetrazole-nitric oxide compds. as enhancing angiotensin II antagonist compds. and their use in treatment of disease)

IT Injury
(vascular wall, treatment of; preparation of benzimidazole-tetrazole-nitric oxide compds. as enhancing angiotensin II antagonist compds. and their use in treatment of disease)

IT Endothelium
(vascular, disease, -induced diseases, treatment of; preparation of benzimidazole-tetrazole-nitric oxide compds. as enhancing angiotensin II antagonist compds. and their use in treatment of disease)

IT Endothelium
(vascular, disease, treatment of; preparation of benzimidazole-tetrazole-nitric oxide compds. as enhancing angiotensin II antagonist compds. and their use in treatment of disease)

IT 52-01-7, Spironolactone 127-07-1, Hydroxyurea 497-27-8, Furoxan 7803-49-8, Hydroxylamine, biological studies 13115-21-4, N-Hydroxyguanidine 14797-55-8, Nitrate, biological studies 14797-65-0, Nitrite, biological studies 20273-10-3, Sydnonimine 29909-71-5, 1,2,3,4-Oxatriazol-5-amine 35576-91-1, Nitrosamide 53414-68-9, Tonin 57842-39-4 66619-03-2, Nitrogen hydride oxide (N2H2O) 103336-05-6, Ditekiren 113082-98-7, Enalkiren 122392-03-4, Medullipin 126222-34-2, Remikiren 138742-43-5, Zankiren 143631-62-3, Ciprokiren 173334-57-1, Aliskiren 909094-11-7, Terlkiren
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of benzimidazole-tetrazole-nitric oxide compds. as enhancing angiotensin II antagonist compds. and their use in treatment of disease)

IT 9015-82-1
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(codrugs; preparation of benzimidazole-tetrazole-nitric oxide compds. as enhancing angiotensin II antagonist compds. and their use in treatment of disease)

IT 52-53-9, Verapamil 58-93-5, Hydrochlorothiazide 77-36-1, Chlorthalidone 86-54-4D, Hydralazine, compds. 304-20-1, Hydralazine hydrochloride 318-98-9, Propranolol hydrochloride 396-01-0, Triamterene 2016-88-8, Amiloride hydrochloride 21829-25-4, Nifedipine 26921-17-5, Timolol maleate 39562-70-4, Nitrendipine 42399-41-7, Diltiazem 55985-32-5, Nicardipine 56392-17-7, Metoprolol tartrate 62571-86-2, Captopril 63675-72-9, Nisoldipine 66085-59-4, Nimodipine 72956-09-3, Carvedilol 75695-93-1, Isradipine 76095-16-4, Enalapril maleate 76547-98-3, Lisinopril 82586-52-5, Moexipril hydrochloride 82586-55-8, Quinapril hydrochloride 86541-74-4, Benazepril hydrochloride 87333-19-5, Ramipril 87679-37-6, Trandolapril 87679-71-8, Trandolaprilat 88150-42-9, Amlodipine 88889-14-9, Fosinopril sodium 104344-23-2, Bisoprolol fumarate 107724-20-9, Eplerenone 133040-01-4D, Eprosartan, derivs., nitrate esters 133240-46-7D, L 158809, derivs., nitrate esters 142999-90-4D, BMS 180560, derivs., nitrate esters 144143-96-4, Eprosartan mesylate 145040-37-5, Candesartan cilexetil 145781-32-4D, Zolasartan, derivs., nitrate esters 146623-69-0D, Saprisartan, derivs., nitrate esters 150802-50-9D, KW 3433, derivs., nitrate esters 153465-66-8D, derivs., nitrate esters
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrugs; preparation of benzimidazole-tetrazole-nitric oxide compds. as

enhancing angiotensin II antagonist compds. and their use in treatment of disease)

IT 924653-67-8P 924653-69-0P 924653-71-4P 924653-73-6P 924653-75-8P 924653-77-0P 924653-79-2P 924653-81-6P 924653-83-8P 924653-85-0P 924653-87-2P 924653-89-4P 924653-91-8P 924653-93-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of benzimidazole-tetrazole-nitric oxide compds. as enhancing angiotensin II antagonist compds. and their use in treatment of disease)

IT 9001-03-0 9015-94-5, Renin, biological studies 50812-31-2, Cyclic nucleotide phosphodiesterase 82707-54-8, Neutral endopeptidase 329900-75-6, Cyclooxygenase-2
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors, codrugs; preparation of benzimidazole-tetrazole-nitric oxide compds. as enhancing angiotensin II antagonist compds. and their use in treatment of disease)

IT 135050-95-2P 138804-35-0P 160514-13-6P 165670-62-2P 165670-63-3P 924653-97-4P 924653-99-6P 924654-01-3P 924654-03-5P 924654-07-9P 924654-09-1P 924654-11-5P 924654-13-7P 924654-15-9P 924654-17-1P 924654-19-3P 924654-21-7P 924654-23-9P 924654-25-1P 924654-27-3P 924654-29-5P 924654-31-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of benzimidazole-tetrazole-nitric oxide compds. as enhancing angiotensin II antagonist compds. and their use in treatment of disease)

IT 52-39-1, Aldosterone 10102-43-9, Nitric oxide, biological studies 139481-59-7D, Candesartan, derivs., nitrate esters
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation of benzimidazole-tetrazole-nitric oxide compds. as enhancing angiotensin II antagonist compds. and their use in treatment of disease)

IT 13408-29-2, Nitroxide 114798-26-4D, Losartan, derivs., nitrate esters 114798-27-5D, derivs., nitrate esters 114798-28-6D, derivs., nitrate esters 114798-29-7D, derivs., nitrate esters 124749-82-2D, derivs., nitrate esters 124749-84-4D, derivs., nitrate esters 124749-85-5D, derivs., nitrate esters 124750-91-0D, derivs., nitrate esters 124750-92-1D, derivs., nitrate esters 124750-93-2D, derivs., nitrate esters 135070-05-2D, derivs., nitrate esters 137862-53-4D, Valsartan, derivs., nitrate esters 137882-98-5D, Abitesartan, derivs., nitrate esters 138402-11-6D, Irbesartan, derivs., nitrate esters 139958-16-0D, derivs., nitrate esters 141309-82-2 143945-39-5D, CL-329167, derivs., nitrate esters 144689-24-7D, Olmesartan, derivs., nitrate esters 144701-48-4D, Telmisartan, derivs., nitrate esters 144702-17-0D, Pomisartan, derivs., nitrate esters 145160-84-5D, derivs., nitrate esters 145216-43-9D, Forasartan, derivs., nitrate esters 145733-36-4D, Tasosartan, derivs., nitrate esters 147403-03-0D, derivs., nitrate esters 148504-51-2D, Ripisartan, derivs., nitrate esters 148564-47-0D, Milfasartan, derivs., nitrate esters 149968-26-3D, Elisartan, derivs., nitrate esters 151406-38-1D, YM-358, derivs., nitrate esters 153235-15-5D, Fonsartan, derivs., nitrate esters 153806-29-2D, derivs., nitrate esters 154749-99-2D, derivs., nitrate esters 155884-08-5D, derivs., nitrate esters 155918-60-8D, derivs., nitrate esters 155918-61-9D, derivs., nitrate esters 156001-18-2D, Embusartan, derivs., nitrate esters 157263-00-8D, MK 996, derivs., nitrate esters 158807-14-8D, derivs., nitrate esters 158807-15-9D, derivs., nitrate esters 158807-16-0D, derivs., nitrate esters 158807-17-1D, derivs., nitrate esters 158807-18-2D, derivs., nitrate esters 158807-19-3D, derivs., nitrate esters 158807-20-6D, derivs.,

nitrate esters 158872-96-9D, derivs., nitrate esters 158872-97-0D, derivs., nitrate esters 159237-67-9D, Enoltasosartan, derivs., nitrate esters 161946-65-2D, derivs., nitrate esters 161947-47-3D, derivs., nitrate esters 161947-48-4D, derivs., nitrate esters 161947-51-9D, derivs., nitrate esters 161947-52-0D, derivs., nitrate esters 161947-55-3D, derivs., nitrate esters 161947-56-4D, derivs., nitrate esters 161947-60-0D, derivs., nitrate esters 161947-61-1D, derivs., nitrate esters 161947-68-8D, derivs., nitrate esters 161947-69-9D, derivs., nitrate esters 161947-70-2D, derivs., nitrate esters 161947-71-3D, derivs., nitrate esters 161947-72-4D, derivs., nitrate esters 161947-74-6D, derivs., nitrate esters 161947-75-7D, derivs., nitrate esters 161947-81-5D, derivs., nitrate esters 161947-82-6D, derivs., nitrate esters 161947-83-7D, derivs., nitrate esters 161947-84-8D, derivs., nitrate esters 161947-85-9D, derivs., nitrate esters 161947-86-0D, derivs., nitrate esters 161947-87-1D, derivs., nitrate esters 161947-88-2D, derivs., nitrate esters 161947-89-3D, derivs., nitrate esters 161947-90-6D, derivs., nitrate esters 161947-91-7D, derivs., nitrate esters 161947-92-8D, derivs., nitrate esters 161947-93-9D, derivs., nitrate esters 161947-94-0D, derivs., nitrate esters 161947-95-1D, derivs., nitrate esters 161947-96-2D, derivs., nitrate esters 161947-97-3D, derivs., nitrate esters 161947-98-4D, derivs., nitrate esters 161947-99-5D, derivs., nitrate esters 161948-00-1D, derivs., nitrate esters 161948-01-2D, derivs., nitrate esters 161948-02-3D, derivs., nitrate esters 165113-01-9D, derivs., nitrate esters 165113-02-0D, derivs., nitrate esters 165113-03-1D, derivs., nitrate esters 165113-04-2D, derivs., nitrate esters 165113-05-3D, derivs., nitrate esters 165113-06-4D, derivs., nitrate esters 165113-07-5D, derivs., nitrate esters 165113-08-6D, derivs., nitrate esters 165113-09-7D, derivs., nitrate esters 165113-10-0D, derivs., nitrate esters 165113-11-1D, derivs., nitrate esters 165113-12-2D, derivs., nitrate esters 165113-13-3D, derivs., nitrate esters 165113-14-4D, derivs., nitrate esters 165113-15-5D, derivs., nitrate esters 165113-16-6D, derivs., nitrate esters 165113-17-7D, derivs., nitrate esters 165113-18-8D, derivs., nitrate esters 165113-19-9D, derivs., nitrate esters 165113-20-2D, derivs., nitrate esters 165113-21-3D, derivs., nitrate esters 165113-22-4D, derivs., nitrate esters 165113-23-5D, derivs., nitrate esters 165113-24-6D, derivs., nitrate esters 165113-25-7D, derivs., nitrate esters 165113-26-8D, derivs., nitrate esters 165113-27-9D, derivs., nitrate esters 165113-28-0D, derivs., nitrate esters 165113-29-1D, derivs., nitrate esters 165113-30-4D, derivs., nitrate esters 165113-31-5D, derivs., nitrate esters 165113-32-6D, derivs., nitrate esters 165113-33-7D, derivs., nitrate esters 165113-34-8D, derivs., nitrate esters 165113-35-9D, derivs., nitrate esters 165113-36-0D, derivs., nitrate esters 165113-37-1D, derivs., nitrate esters 165113-38-2D, derivs., nitrate esters 165113-39-3D, derivs., nitrate esters 165113-40-6D, derivs., nitrate esters 165113-41-7D, derivs., nitrate esters 165113-42-8D, derivs., nitrate esters 165113-43-9D, derivs., nitrate esters 165113-44-0D, derivs., nitrate esters 165113-45-1D, derivs., nitrate esters 165113-46-2D, derivs., nitrate esters 165113-47-3D, derivs., nitrate esters 165113-48-4D, derivs., nitrate esters 165113-49-5D, derivs., nitrate esters 165113-50-8D, derivs., nitrate esters 165113-51-9D, derivs., nitrate esters 165113-52-0D, derivs., nitrate esters 165113-53-1D, derivs., nitrate esters 165113-54-2D, derivs., nitrate esters 165113-55-3D, derivs., nitrate esters 165113-56-4D, derivs., nitrate esters 165113-57-5D, derivs., nitrate esters 165113-58-6D, derivs., nitrate esters 165113-59-7D, derivs., nitrate esters 165113-60-0D, derivs., nitrate esters 165113-61-1D, derivs., nitrate esters 165113-62-2D, derivs., nitrate esters 165113-63-3D, derivs., nitrate esters 165113-64-4D, derivs., nitrate esters 165113-65-5D, derivs., nitrate esters 165113-66-6D,

derivs., nitrate esters 165113-67-7D, derivs., nitrate esters 165113-68-8D, derivs., nitrate esters 165113-69-9D, derivs., nitrate esters 165113-70-2D, derivs., nitrate esters 165113-71-3D, derivs., nitrate esters 165113-72-4D, derivs., nitrate esters 165113-73-5D, derivs., nitrate esters 165113-74-6D, derivs., nitrate esters 166813-82-7D, derivs., nitrate esters 166961-56-4D, derivs., nitrate esters 166961-58-6D, derivs., nitrate esters 167301-42-0D, derivs., nitrate esters 167371-59-7D, derivs., nitrate esters 168686-32-6D, derivs., nitrate esters 169281-89-4D, derivs., nitrate esters 177848-35-0D, derivs., nitrate esters 207400-83-7D, Glycyllosartan, derivs., nitrate esters 223926-77-0D, derivs., nitrate esters 244126-99-6D, derivs., nitrate esters 272438-16-1D, derivs., nitrate esters 272446-75-0D, derivs., nitrate esters 439904-54-8D, derivs., nitrate esters 439904-55-9D, derivs., nitrate esters 439904-56-0D, derivs., nitrate esters 439904-57-1D, derivs., nitrate esters 439904-58-2D, derivs., nitrate esters 439904-65-1D, derivs., nitrate esters

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(preparation of benzimidazole-tetrazole-nitric oxide compds. as enhancing angiotensin II antagonist compds. and their use in treatment of disease)

IT 137862-53-4, Valsartan 139481-59-7, Candesartan

RL: PAC (Pharmacological activity); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)

(starting material; preparation of benzimidazole-tetrazole-nitric oxide compds. as enhancing angiotensin II antagonist compds. and their use in treatment of disease)

IT 76-83-5, Trityl chloride 638-29-9, Valeroyl chloride 2154-67-8 13518-40-6 21569-01-7 37149-18-1 65141-52-8 74754-55-5 74754-56-6 104963-92-0 145004-89-3 145459-16-1 165670-58-6 646511-09-3 849113-53-7 861405-30-3

RL: RCT (Reactant); RACT (Reactant or reagent)

(starting material; preparation of benzimidazole-tetrazole-nitric oxide compds. as enhancing angiotensin II antagonist compds. and their use in treatment of disease)

L23 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2008 ACS on STN

IT 13408-29-2, Nitroxide

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(heterocyclic nitric oxide donor groups as diuretics)

RN 13408-29-2 CAPLUS

CN Nitroxide (7CI, 8CI, 9CI) (CA INDEX NAME)

ACCESSION NUMBER: 2006:494118 CAPLUS

DOCUMENT NUMBER: 145:1033

TITLE: Diuretic compounds comprising heterocyclic nitric oxide donor groups, compositions and methods of use

INVENTOR(S): Garvey, David S.; Ranatunge, Ramani R.

PATENT ASSIGNEE(S): Nitromed, Inc., USA

SOURCE: PCT Int. Appl., 87 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006055542	A2	20060526	WO 2005-US41321	20051115
WO 2006055542	A3	20060908		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

AU 2005306629	A1	20060526	AU 2005-306629	20051115
CA 2574535	A1	20060526	CA 2005-2574535	20051115
EP 1828155	A2	20070905	EP 2005-851657	20051115

R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR

PRIORITY APPLN. INFO.:	US 2004-627177P	P	20041115
	US 2005-656546P	P	20050228
	US 2005-692231P	P	20050621
	WO 2005-US41321	W	20051115

OTHER SOURCE(S): MARPAT 145:1033

AN 2006:494118 CAPLUS

DN 145:1033

ED Entered STN: 26 May 2006

TI Diuretic compounds comprising heterocyclic nitric oxide donor groups, compositions and methods of use

IN Garvey, David S.; Ranatunge, Ramani R.

PA Nitromed, Inc., USA

SO PCT Int. Appl., 87 pp.
CODEN: PIXXD2

DT Patent

LA English

CC 1-8 (Pharmacology)
Section cross-reference(s): 28

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2006055542	A2	20060526	WO 2005-US41321	20051115
WO 2006055542	A3	20060908		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

AU 2005306629	A1	20060526	AU 2005-306629	20051115
CA 2574535	A1	20060526	CA 2005-2574535	20051115
EP 1828155	A2	20070905	EP 2005-851657	20051115

R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,

IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR

PRAI US 2004-627177P P 20041115
US 2005-656546P P 20050228
US 2005-692231P P 20050621
WO 2005-US41321 W 20051115

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2006055542	IPCI	A61K0031-541 [I,A]; C07D0285-00 [I,C]; A61K0031-41 [I,C]; A61K0031-5375 [I,C]; A61K0031-54 [I,C]; C07D0269-00 [I,C]; C07D0295-00 [I,C]; C07D0285-16 [I,A]; A61K0031-41 [I,A]; A61K0031-5375 [I,A]; A61K0031-54 [I,A]; C07D0269-00 [I,A]; C07D0295-00 [I,A]
	IPCR	A61K0031-541 [I,A]; A61K0031-541 [I,C]
AU 2005306629	IPCI	A61K0031-541 [I,C]; A61K0031-541 [I,A]
CA 2574535	IPCI	A61K0031-41 [I,A]; A61K0031-5375 [I,A]; A61K0031-54 [I,A]; C07D0269-00 [I,A]; C07D0285-16 [I,A]; C07D0285-00 [I,C*]; C07D0295-00 [I,A]
	IPCR	C07D0285-00 [I,C]; C07D0285-16 [I,A]; A61K0031-41 [I,C]; A61K0031-41 [I,A]; A61K0031-5375 [I,C]; A61K0031-5375 [I,A]; A61K0031-54 [I,C]; A61K0031-54 [I,A]; C07D0269-00 [I,C]; C07D0269-00 [I,A]; C07D0295-00 [I,C]; C07D0295-00 [I,A]
EP 1828155	IPCI	C07D0285-16 [I,A]; C07D0285-00 [I,C*]; C07D0295-00 [I,A]; C07D0269-00 [I,A]; A61K0031-41 [I,A]; A61K0031-5375 [I,A]; A61K0031-54 [I,A]
	IPCR	C07D0285-00 [I,C]; C07D0285-16 [I,A]; A61K0031-41 [I,C]; A61K0031-41 [I,A]; A61K0031-5375 [I,C]; A61K0031-5375 [I,A]; A61K0031-54 [I,C]; A61K0031-54 [I,A]; C07D0269-00 [I,C]; C07D0269-00 [I,A]; C07D0295-00 [I,C]; C07D0295-00 [I,A]

OS MARPAT 145:1033

AB The invention describes novel diuretic compds. comprising at least one heterocyclic nitric oxide donor group, or pharmaceutically acceptable salts thereof, and novel composition comprising at least one diuretic compound comprising at least one heterocyclic nitric oxide donor group, and optionally, at least one nitric oxide enhancing compound and/or at least one therapeutic agent. The invention also provides novel compns. and kits comprising at least one diuretic compound of the invention comprising at least one heterocyclic nitric oxide donor group, and optionally, at least one nitric oxide enhancing compound and/or at least one therapeutic agent. The invention also provides methods for (a) treating conditions resulting from excessive water and/or electrolyte retention; (b) treating cardiovascular diseases; (c) treating renovascular diseases; (d) treating diabetes; (e) treating diseases resulting from oxidative stress; (f) treating endothelial dysfunctions; (g) treating diseases caused by endothelial dysfunctions; (h) treating cirrhosis; (j) treating pre-eclampsia; (k) treating osteoporosis; (1) treating nephropathy; (m) treating peripheral vascular diseases; (n) treating portal hypertension; (o) treating central nervous system disorders; and (p) treating sexual dysfunctions. The heterocyclic nitric oxide donors are preferably furoxans, sydnonimines, oxatriazole-5-ones and/or oxatriazole-5-imines.

ST diuretic nitric oxide donor cardiovascular disease therapy

IT Antihistamines
(H2; heterocyclic nitric oxide donor groups as diuretics)

IT Ear, disease
(Meniere's, edema associated with; heterocyclic nitric oxide donor groups as diuretics)

IT Thiols, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(S-nitroso; heterocyclic nitric oxide donor groups as diuretics)
IT Platelet (blood)
(adhesion; heterocyclic nitric oxide donor groups as diuretics)
IT Heart, disease
(angina pectoris, unstable; heterocyclic nitric oxide donor groups as diuretics)
IT Endothelin receptors
Mineralocorticoid receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antagonists; heterocyclic nitric oxide donor groups as diuretics)
IT Heart, disease
(arrhythmia; heterocyclic nitric oxide donor groups as diuretics)
IT Hyperplasia
(arterial intimal; heterocyclic nitric oxide donor groups as diuretics)
IT Edema
(associated with heart failure, cirrhosis, nephritis, premenstrual syndrome, hypertension, Meniere's disease, glaucoma, cystic fibrosis and sodium, potassium imbalance; heterocyclic nitric oxide donor groups as diuretics)
IT Wound
(associated with use of medical device; heterocyclic nitric oxide donor groups as diuretics)
IT Heart, disease
(atrial fibrillation; heterocyclic nitric oxide donor groups as diuretics)
IT Heart, disease
(atrial flutter; heterocyclic nitric oxide donor groups as diuretics)
IT Ischemia
(cardiac; heterocyclic nitric oxide donor groups as diuretics)
IT Edema
Ischemia
(cerebral; heterocyclic nitric oxide donor groups as diuretics)
IT Brain, disease
(cerebrovascular; heterocyclic nitric oxide donor groups as diuretics)
IT Inflammation
Kidney, disease
(chronic nephritis, edema associated with; heterocyclic nitric oxide donor groups as diuretics)
IT Artery
(coronary, plaque inflammation; heterocyclic nitric oxide donor groups as diuretics)
IT Artery, disease
(coronary; heterocyclic nitric oxide donor groups as diuretics)
IT Heart, disease
(diastolic dysfunction, enlargement; heterocyclic nitric oxide donor groups as diuretics)
IT Natural products, pharmaceutical
(digitalis; heterocyclic nitric oxide donor groups as diuretics)
IT Contraceptives
(edema associated with use of; heterocyclic nitric oxide donor groups as diuretics)
IT Cirrhosis
Glaucoma (disease)
Hypertension
Malnutrition
Sunburn
(edema associated with; heterocyclic nitric oxide donor groups as diuretics)
IT Brain, disease
Lung, disease
(edema; heterocyclic nitric oxide donor groups as diuretics)

IT Blood vessel, disease
(endothelium; heterocyclic nitric oxide donor groups as diuretics)
IT Electrolytes, biological
(excess, retention; heterocyclic nitric oxide donor groups as diuretics)
IT Heart, disease
Lymphatic system, disease
(failure, edema associated with; heterocyclic nitric oxide donor groups as diuretics)
IT Kidney, disease
(failure; heterocyclic nitric oxide donor groups as diuretics)
IT Blood vessel
(grafting; heterocyclic nitric oxide donor groups as diuretics)
IT Aneurysm
Angiotensin receptor antagonists
Anticoagulants
Antidiabetic agents
Antihypertensives
Antioxidants
Atherosclerosis
Calcium channel blockers
Cardiovascular agents
Cardiovascular system, disease
Central nervous system, disease
Central nervous system agents
Combination chemotherapy
Coronary angioplasty
Coronary bypass surgery
Cystic fibrosis
Diuretics
Drug delivery systems
Fatigue, biological
Human
Hypercholesterolemia
Hyperlipidemia
Hypolipemic agents
Kidney, disease
Osteoporosis
Oxidative stress, biological
Platelet aggregation
Platelet aggregation inhibitors
Potassium channel blockers
Preeclampsia
Sexual disorders
Shock (circulatory collapse)
Swelling, biological
Thrombosis
Vasodilators
α-Adrenoceptor antagonists
β-Adrenoceptor antagonists
(heterocyclic nitric oxide donor groups as diuretics)
IT Oximes
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(heterocyclic nitric oxide donor groups as diuretics)
IT Brain, disease
Heart, disease
(infarction; heterocyclic nitric oxide donor groups as diuretics)
IT Artery, disease
(intima, hyperplasia; heterocyclic nitric oxide donor groups as diuretics)

IT Brain, disease
Heart, disease
(ischemia; heterocyclic nitric oxide donor groups as diuretics)
IT Anti-inflammatory agents
(nonsteroidal; heterocyclic nitric oxide donor groups as diuretics)
IT Blood vessel, disease
(peripheral; heterocyclic nitric oxide donor groups as diuretics)
IT Adhesion, biological
(platelet; heterocyclic nitric oxide donor groups as diuretics)
IT Circulation
(poor, edema associated with; heterocyclic nitric oxide donor groups as diuretics)
IT Hypertension
(portal; heterocyclic nitric oxide donor groups as diuretics)
IT Ovarian cycle
(premenstrual syndrome, edema associated with; heterocyclic nitric oxide donor groups as diuretics)
IT Transport proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(proton pump, inhibitors; heterocyclic nitric oxide donor groups as diuretics)
IT Edema
(pulmonary; heterocyclic nitric oxide donor groups as diuretics)
IT Artery, disease
(restenosis, postangioplasty; heterocyclic nitric oxide donor groups as diuretics)
IT Body fluid
(retention; heterocyclic nitric oxide donor groups as diuretics)
IT Respiratory air
(shortness of breath; heterocyclic nitric oxide donor groups as diuretics)
IT Cell proliferation
(smooth muscle; heterocyclic nitric oxide donor groups as diuretics)
IT Brain, disease
(stroke; heterocyclic nitric oxide donor groups as diuretics)
IT Leg
(swelling; heterocyclic nitric oxide donor groups as diuretics)
IT Embolism
(thromboembolism; heterocyclic nitric oxide donor groups as diuretics)
IT Medical goods
(vascular or non-vascular complication associated with; heterocyclic nitric oxide donor groups as diuretics)
IT Endothelium
(vascular, disease; heterocyclic nitric oxide donor groups as diuretics)
IT 10102-43-9, Nitric oxide, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(donors; heterocyclic nitric oxide donor groups as diuretics)
IT 7732-18-5, Water, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(excess, retention; heterocyclic nitric oxide donor groups as diuretics)
IT 3086-91-7P 887602-54-2P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(heterocyclic nitric oxide donor groups as diuretics)
IT 887602-55-3P 887602-58-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

(Uses)
(heterocyclic nitric oxide donor groups as diuretics)
IT 52-01-7, Spironolactone 58-54-8, Ethacrynic acid 58-93-5, Hydrochlorothiazide 58-94-6, Chlorothiazide 73-48-3, Bendroflumethiazide 73-49-4, Quinethazone 77-36-1, Chlorothalidone 86-54-4D, Hydralazine, derivs. 91-33-8, Benzthiazide 121-30-2, Chloraminophenamide 127-07-1, Hydroxyurea 133-67-5, Trichloromethiazide 135-07-9 135-09-1, Hydroflumethiazide 304-20-1, Hydralazine hydrochloride 318-98-9, Propranolol hydrochloride 346-18-9, Polythiazide 396-01-0, Triamterene 497-27-8, Furoxan 636-54-4, Clopamide 671-88-5, Disulfamide 671-95-4, Clofenamide 1580-83-2, Paraflutizide 1824-58-4, Ethiazide 2016-88-8, Amiloride hydrochloride 2043-38-1, Buthiazide 2259-96-3, Cyclothiazide 3754-19-6, Ambuside 4267-05-4, Teclothiazide 5588-16-9, Althiazide 7195-27-9, Mefruside 7803-49-8, Hydroxylamine, biological studies 13115-21-4, N-Hydroxyguanidine 13408-29-2, Nitroxide 14293-44-8, Xipamide 14448-38-5, Hyponitrous acid 14797-55-8, Nitrate, biological studies 14797-65-0, Nitrite, biological studies 17560-51-9, Metolazone 20273-10-3, 1,2,3-Oxadiazol-5-amine 20287-37-0, Fenquizone 26921-17-5, Timolol maleate 27589-33-9, Azosemide 28395-03-1 35576-91-1, Nitrosamide 40180-04-9, Ticrynafen 55837-27-9, Piretanide 56392-17-7, Metoprolol tartrate 57842-39-4 62571-86-2, Captopril 66619-03-2, Nitrosimine 72956-09-3, Carvedilol 76095-16-4, Enalapril maleate 76547-98-3, Lisinopril 82586-52-5, Moexipril hydrochloride 82586-55-8, Quinapril hydrochloride 82875-49-8 86541-74-4, Benazepril hydrochloride 87333-19-5, Ramipril 87679-37-6, Trandolapril 87679-71-8, Trandolaprilat 88889-14-9, Fosinopril sodium 104344-23-2, Bisoprolol fumarate 107724-20-9, Eplerenone 124750-99-8, Losartan potassium 137862-53-4, Valsartan 138402-11-6, Irbesartan 144143-96-4, Eprosartan mesylate 144689-63-4, Olmesartan Medoxomil 144701-48-4, Telmisartan 145040-37-5, Candesartan cilexetil 887602-60-0 887602-61-1 887602-62-2 887602-63-3 887602-64-4 887602-65-5 887602-66-6 887602-67-7
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(heterocyclic nitric oxide donor groups as diuretics)
IT 54-31-9, Furosemide 183537-57-7 220270-86-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(heterocyclic nitric oxide donor groups as diuretics)
IT 9000-83-3, ATPase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(hydrogen ion-translocating, inhibitors; heterocyclic nitric oxide donor groups as diuretics)
IT 7440-09-7, Potassium, biological studies 7440-23-5, Sodium, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(imbalance, edema associated with; heterocyclic nitric oxide donor groups as diuretics)
IT 9015-82-1 9015-94-5, Renin, biological studies 50812-31-2 82707-54-8, Neutral endopeptidase 329900-75-6, Cyclooxygenase-2
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; heterocyclic nitric oxide donor groups as diuretics)

L23 ANSWER 8 OF 8 MEDLINE on STN
ACCESSION NUMBER: 2007019497 MEDLINE
DOCUMENT NUMBER: PubMed ID: 16718449
TITLE: Tempol prevents harmful effects of remote ischemia reperfusion injury on healing of experimental colonic anastomoses.
AUTHOR: Aydin Cagatay; Teke Zafer; Aytekin Faruk; Yenisey Cigdem; Kabay Burhan; Simsek Nilufer Genc; Tekin Koray

CORPORATE SOURCE: Faculty of Medicine, Genel Cerrahi Anabilim Dali, Kinikli, Pamukkale University, Denizli, 20070, Turkey.. cagatayaydin@yahoo.com
SOURCE: International journal of colorectal disease, (2007 Mar) Vol. 22, No. 3, pp. 325-31. Electronic Publication: 2006-05-23.
Journal code: 8607899. ISSN: 0179-1958.
PUB. COUNTRY: Germany: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200711
ENTRY DATE: Entered STN: 12 Jan 2007
Last Updated on STN: 7 Dec 2007
Entered Medline: 27 Nov 2007
AN 2007019497 MEDLINE
DN PubMed ID: 16718449
TI Tempol prevents harmful effects of remote ischemia reperfusion injury on healing of experimental colonic anastomoses.
AU Aydin Cagatay; Teke Zafer; Aytekin Faruk; Yenisey Cigdem; Kabay Burhan; Simsek Nilufer Genc; Tekin Koray
CS Faculty of Medicine, Genel Cerrahi Anabilim Dali, Kinikli, Pamukkale University, Denizli, 20070, Turkey.. cagatayaydin@yahoo.com
SO International journal of colorectal disease, (2007 Mar) Vol. 22, No. 3, pp. 325-31. Electronic Publication: 2006-05-23.
Journal code: 8607899. ISSN: 0179-1958.
CY Germany: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200711
ED Entered STN: 12 Jan 2007
Last Updated on STN: 7 Dec 2007
Entered Medline: 27 Nov 2007
AB BACKGROUND AND AIMS: Tempol (4-hydroxy-2,2,6,6-tetramethylpiperidine-N-oxyl) is a water-soluble analogue of the spin label TEMPO. As an antioxidative agent, it is a member of nitroxides, which detoxifies superoxide and possibly other toxic radicals in vivo. In this study, we aimed to investigate whether tempol prevents harmful systemic effects of superior mesenteric ischemia-reperfusion on left colonic anastomosis in rats. MATERIALS AND METHODS: Anastomosis of the left colon was performed in 30 rats that were divided into three groups each having ten animals: sham-operated control (group I), 60 min of intestinal ischemia-reperfusion by superior mesenteric artery occlusion (group II), and tempol-treated group (30 mg/kg before and after the ischemia-reperfusion (group III). On postoperative day 5, all animals were killed and anastomotic bursting pressures were measured in vivo. Tissue samples were obtained for further investigation of anastomotic hydroxyproline content, perianastomotic malondialdehyde, and glutathione levels. RESULTS: There was a statistically significant increase in the quantity of myeloperoxidase activity and malondialdehyde levels in group II, along with a decrease in glutathione levels, anastomotic hydroxyproline content, and bursting pressure values when compared to controls. However, all of the investigated parameters were normalized in tempol-treated animals (group III). CONCLUSION: We conclude that tempol significantly prevents harmful systemic effects of reperfusion injury on colonic anastomoses in a rat model of superior mesenteric artery occlusion.
CT Check Tags: Male
Anastomosis, Surgical
Animals

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     *Antioxidants: PD, pharmacology
      Antioxidants: TU, therapeutic use
       *Colon: SU, surgery
      Constriction
     *Cyclic N-Oxides: PD, pharmacology
      Cyclic N-Oxides: TU, therapeutic use
      Disease Models, Animal
        Mesenteric Artery, Superior: SU, surgery
      Rats
      Rats, Wistar
     *Reperfusion Injury: PC, prevention & control
      Spin Labels
     *Wound Healing: DE, drug effects
RN   2226-96-2 (tempol)
CN   0 (Antioxidants); 0 (Cyclic N-Oxides); 0 (Spin Labels)


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     (FILE 'HOME' ENTERED AT 11:38:10 ON 03 MAR 2008)

     FILE 'REGISTRY' ENTERED AT 11:38:21 ON 03 MAR 2008

     FILE 'CAPLUS' ENTERED AT 11:39:58 ON 03 MAR 2008
                E US2006-554299/APPS
L1              1 S E3
                  SEL RN L1

     FILE 'REGISTRY' ENTERED AT 11:41:25 ON 03 MAR 2008
L2              2 S E1-E2
L3              1 S 13408-29-2
L4              1 S 2226-96-2

     FILE 'CAPLUS, BIOSIS, EMBASE, MEDLINE' ENTERED AT 11:42:52 ON 03 MAR 2008
L5           7167 S L3 OR L4
                  E ISCHEMIA
L6         511008 S E3
                  E ADMINISTRATION
L7        4202108 S E3
L8           1552 S (("MEDICAL TREATMENT") OR ("MEDICAL PROCEDURE?")) AND L6
L9              0 S L8 AND L5
L10             0 S L5 AND L8
L11           245 S L5 AND ISCHEMIA
L12            63 S L11 AND ADMINISTRATION
L13            28 S L12 AND (INTRAVENOUS OR PARENTERAL)
L14             9 S L12 AND ((ORAL OR ORALLY) OR ("BY MOUTH"))
L15             4 S L14 AND L13
L16       8476811 S  S
L17             0 S L15 AND SURGERY
L18             0 S L14 AND SURGERY
L19             1 S L13 AND SURGERY
L20             1 S L12 AND SURGERY
L21             8 S L11 AND SURGERY
L22             4 S L5 AND SURGERY AND INTRAVENOUS
L23             8 DUP REM L22 L21 (4 DUPLICATES REMOVED)

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